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| | | | |
|---|---|---|---|
| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS | 2 | AUG 06 | CAS REGISTRY enhanced with new experimental property tags |
| NEWS | 3 | AUG 06 | FSTA enhanced with new thesaurus edition |
| NEWS | 4 | AUG 13 | CA/CAplus enhanced with additional kind codes for granted patents |
| NEWS | 5 | AUG 20 | CA/CAplus enhanced with CAS indexing in pre-1907 records |
| NEWS | 6 | AUG 27 | Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB |
| NEWS | 7 | AUG 27 | USPATOLD now available on STN |
| NEWS | 8 | AUG 28 | CAS REGISTRY enhanced with additional experimental spectral property data |
| NEWS | 9 | SEP 07 | STN AnaVist, Version 2.0, now available with Derwent World Patents Index |
| NEWS | 10 | SEP 13 | FORIS renamed to SOFIS |
| NEWS | 11 | SEP 13 | INPADOCDB enhanced with monthly SDI frequency |
| NEWS | 12 | SEP 17 | CA/CAplus enhanced with printed CA page images from 1967-1998 |
| NEWS | 13 | SEP 17 | CAplus coverage extended to include traditional medicine patents |
| NEWS | 14 | SEP 24 | EMBASE, EMBAL, and LEMBASE reloaded with enhancements |
| NEWS | 15 | OCT 02 | CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt |
| NEWS | 16 | OCT 19 | BEILSTEIN updated with new compounds |
| NEWS | 17 | NOV 15 | Derwent Indian patent publication number format enhanced |
| NEWS | 18 | NOV 19 | WPIX enhanced with XML display format |
| NEWS | 19 | NOV 30 | ICSD reloaded with enhancements |
| NEWS | 20 | DEC 04 | LINPADOCDB now available on STN |
| NEWS | 21 | DEC 14 | BEILSTEIN pricing structure to change |
| NEWS | 22 | DEC 17 | USPATOLD added to additional database clusters |
| NEWS | 23 | DEC 17 | IMSDRUGCONF removed from database clusters and STN |
| NEWS | 24 | DEC 17 | DGENE now includes more than 10 million sequences |
| NEWS | 25 | DEC 17 | TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment |
| NEWS | 26 | DEC 17 | MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary |
| NEWS | 27 | DEC 17 | CA/CAplus enhanced with new custom IPC display formats |
| NEWS | 28 | DEC 17 | STN Viewer enhanced with full-text patent content from USPATOLD |

NEWS EXPRESS  19 SEPTEMBER 2007:  CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

| | |
|---|---|
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                                                         ENTRY    SESSION
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DICTIONARY FILE UPDATES:  26 DEC 2007  HIGHEST RN 959588-76-2

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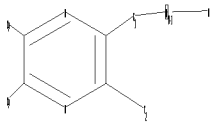
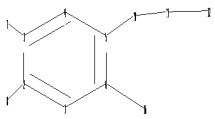




chain nodes :
7 8 10 11 12 16
ring nodes :
1 2 3 4 5 6
chain bonds :
2-8 3-7 5-10 6-16 10-11 11-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
2-8 3-7 5-10 6-16 10-11 11-12
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:C,S

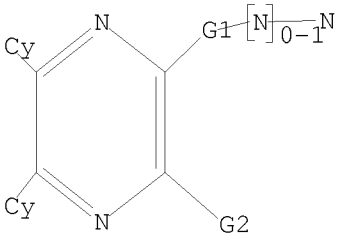
G2:C,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 10:CLASS 11:CLASS
12:CLASS 16:CLASS
Generic attributes :
7:
Saturation : Unsaturated
8:
Saturation : Unsaturated

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS

L1 STR




G1 C,S

G2 C,O,N

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 09:47:44 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 6907 TO ITERATE

29.0% PROCESSED 2000 ITERATIONS 4 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 133158 TO 143122
PROJECTED ANSWERS: 53 TO 499

L2 4 SEA SSS SAM L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY 0.45 TOTAL SESSION 0.66
FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 09:47:52 ON 27 DEC 2007
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FILE COVERS 1907 - 27 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007 (20071226/ED)

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=> s l2
L3           4 L2

=> d 1-4 ibib abs

L3   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2005:962046  CAPLUS
DOCUMENT NUMBER:         143:266952
TITLE:                   Preparation of bipyridyl amides as modulators of
                         metabotropic glutamate receptor-5
INVENTOR(S):             Bonnefous, Celine; Kamenecka, Theodore M.; Vernier,
                         Jean-Michel
PATENT ASSIGNEE(S):      Merck & Co., Inc., USA
SOURCE:                  PCT Int. Appl., 79 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2005079802         A1    20050901    WO 2005-US3952          20050209
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     AU 2005215379         A1    20050901    AU 2005-215379          20050209
     CA 2555402            A1    20050901    CA 2005-2555402         20050209
     EP 1715867            A1    20061102    EP 2005-713111          20050209
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
     CN 1933838            A     20070321    CN 2005-80004732        20050209
     JP 2007524682         T     20070830    JP 2006-553189          20050209
     IN 2006DN04346        A     20070713    IN 2006-DN4346          20060727
     US 2007149547         A1    20070628    US 2006-589407          20060811
PRIORITY APPLN. INFO.:                       US 2004-544627P     P   20040212
                                             WO 2005-US3952      W   20050209
OTHER SOURCE(S):         CASREACT 143:266952; MARPAT 143:266952
GI
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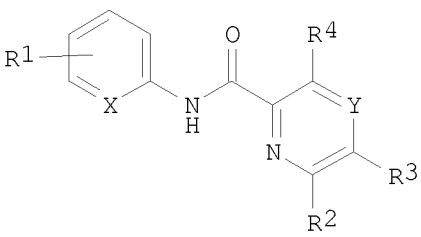


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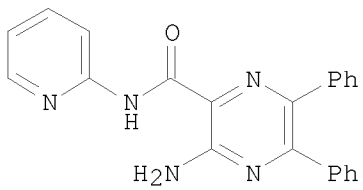


II

AB The title compds. I [X = N, C; Y = N, C, C(halo); R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl, aryl, etc.; R3 = aryl, halo, alkyl, etc.; R2 and R3 may be joined together with the atoms to which they are attached to form a (un)saturated 4-7 membered ring containing 0-2 heteroatoms selected from O, S and N; R4 = aryl, heteroaryl, halo, etc.] which are mGluR5 modulators useful in the treatment or prevention of diseases and conditions in which mGluR5 is involved, including but not limited to psychiatric and mood disorders such as schizophrenia, anxiety, depression, bipolar disorders, and panic, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm and sleep disorders, such as shift-work induced sleep disorder and jet-lag, drug addiction, drug abuse, drug withdrawal, obesity and other diseases, were prepared Thus, amidation of pyridin-2-amine with 3-amino-5,6-diphenylpyrazine-2-carboxylic acid afforded the amide II. The exemplified compds. I have mGluR5 inhibitory activity as shown by inhibition at 10 μM or less in the calcium flux assay or 100 μM or less or less in the PI assay. The invention is also directed to pharmaceutical compns. comprising compds. I.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127366 CAPLUS
DOCUMENT NUMBER: 142:56362
TITLE: Preparation of 3-substituted 5,6-diaryl-pyrazine-2-carboxamide and 2-sulfonamide derivatives as cannabinoid receptor 1 (CB1) modulators
INVENTOR(S): Cheng, Leifeng
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004111034 | A1 | 20041223 | WO 2004-SE970 | 20040616 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004247616 | A1 | 20041223 | AU 2004-247616 | 20040616 |
| CA 2527035 | A1 | 20041223 | CA 2004-2527035 | 20040616 |
| EP 1638953 | A1 | 20060329 | EP 2004-749012 | 20040616 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| BR 2004011508 | A | 20060725 | BR 2004-11508 | 20040616 |
| CN 1809554 | A | 20060726 | CN 2004-80017200 | 20040616 |
| JP 2006527771 | T | 20061207 | JP 2006-517044 | 20040616 |
| NO 2005005919 | A | 20060216 | NO 2005-5919 | 20051213 |
| MX 2005PA13711 | A | 20060308 | MX 2005-PA13711 | 20051215 |
| US 2007093484 | A1 | 20070426 | US 2005-560862 | 20051215 |
| PRIORITY APPLN. INFO.: | | | GB 2003-14057 A | 20030618 |

WO 2004-SE970 W 20040616

OTHER SOURCE(S): MARPAT 142:56362

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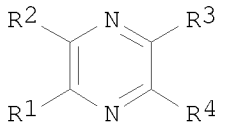

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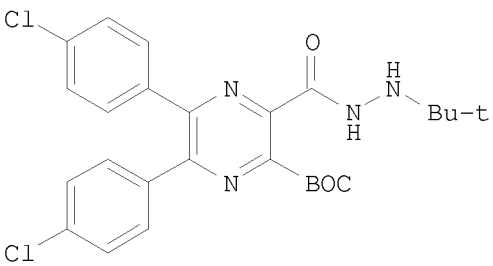


II

AB Title compds. I [wherein R1, R2 = independently (un)substituted Ph, thienyl, pyridinyl; R3 = X-Y-NR5R6; X = absent, CO, or SO2; Y = absent, NH optionally substituted by an alkyl group; R5, R6 = independently (un)substituted amino/alkyl, (CH2)r(phenyl)s, (un)saturated 5-8-membered heterocyclyl; R5 = H and R6 = defined above; or R5NR6 = (un)substituted (un)saturated 5-8-membered heterocyclyl; r = 0-4; s = 1 when r = 0, otherwise s = 1 or 2; R5NR6 = (un)substituted (un)saturated 5-8-membered heterocyclyl; R4 = (CH2)nCO2R7; n = 0-4; R7 = (un)substituted cycloalkyl/cyclo/alkyl, (CH2)nphenyl, saturated or partially unsatd. 5-8-membered heterocyclyl, CONH2 and derivs.; n = defined as above; and pharmaceutically acceptable salts thereof] were prepared as cannabinoid 1 (CB1) receptor modulators. For example, reacting 3-(tert-butoxycarbonyl)-5,6-bis(4-chlorophenyl)pyrazine-2-carboxylic acid (preparation given) with tert-butylhydrazine hydrochloride gave pyrazine II. I are active at the CB1 receptor (IC50 < 1 μM), most preferred compds. have IC50 < 200 nM. For instance, II exhibited an IC50 (hCB1) = 1.8 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of obesity, psychiatric and neurol. disorders (no data).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1980:41887 CAPLUS

DOCUMENT NUMBER: 92:41887

ORIGINAL REFERENCE NO.: 92:6993a,6996a

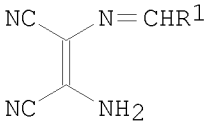
TITLE: Chemistry of diaminomaleonitrile. 5. Dihydropyrazine synthesis

AUTHOR(S): Ohtsuka, Yozo; Tohma, Eiko; Kojima, Sigeru; Tomita, Nobuo

CORPORATE SOURCE: Sagami Chem. Res. Cent., Sagamihara, 229, Japan

SOURCE: Journal of Organic Chemistry (1979), 44(26), 4871-6
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 92:41887
GI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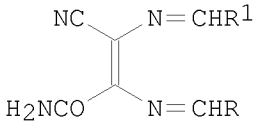
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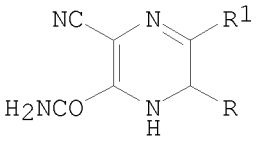
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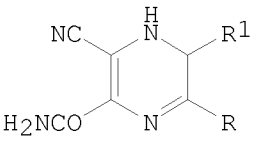

IV

AB Condensation of RCHO (R = optionally substituted Ph) with Schiff bases I (R1 = optionally substituted Ph, CHMe2) in the presence of NEt3 <20° is accompanied by regiospecific hydration of the nitrile groups to give 3-cyanoacrylamide derivs. II, which cyclize readily into 1,2-dihydropyrazines III and IV. The substituent effect on the product ratio is examined, and the reaction mechanism is discussed in terms of a new general reaction pattern of diaminomaleonitrile derivative Reactions of III and IV by oxidation, reduction, hydantoin formation with isocyanates, and cyanoethylation are also reported.

L3 ANSWER 4 OF 4 CAPLUS 
ACCESSION NUMBER: 1956:69468 CAPLUS
DOCUMENT NUMBER: 50:69468
ORIGINAL REFERENCE NO.: 50:13047b-i,13048a-b
TITLE: Pteridines. XIV. Further studies on a new approach to pteridine synthesis
AUTHOR(S): Taylor, E. C., Jr.; Garland, Robert B.; Howell, Charles F.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1956), 78, 210-13
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:69468

AB cf. C.A. 50, 2608h. 3-Amino-5,6-diphenylpyrazinamide (I) (1.509 g.) and 10 cc. BzCl refluxed 4 h., cooled, and diluted with 250 cc. petr. ether gave 1.179 g. 2,6,7-triphenyl-4(3H)-pteridinone (II), white needles, m. 290° (from CH2Cl2-petr. ether and then aqueous HCONMe2) (all m.ps. are corrected). The N-PhCH2 derivative (III) of I (0.5 g.) and 25 cc. AcCl refluxed 4 h. and diluted with 25 cc. petr. ether yielded 0.36 g. 3-acetylamino-5,6-diphenylpyrazinamide (IV), bright yellow platelets, m. 207-8° (from CHCl3-petr. ether). III (0.835 g.), 10 cc. Ac2O, and 10 cc. MeCN refluxed 4 h. and evaporated to dryness in vacuo, and the residue treated with EtOH and evaporated to dryness again gave 0.472 g. N-PhCH2 derivative (V) of IV, tan crystals, m. 149-50° (from CH2Cl2-petr. ether). V (0.613 g.) refluxed 3 h. with 0.5 g. Na in 10 cc. absolute EtOH and poured into 50 cc. H2O gave 0.503 g. III, m. 186-7°. 3-PhCH2 derivative of II gave similarly 93% III. I (2.53 g.), 5 cc. PhNCO, and 25 cc. dry pyridine refluxed 1 h. and cooled yielded 2.81 g. 3-(3-phenylureido)-5,6-diphenylpyrazinamide (VI), light yellow platelets, m. 240.5-1.5°

(from aqueous EtOH and then aqueous HCONMe2). III (0.80 g.), 1 cc. PhNCO, and 10 cc. dry pyridine refluxed 2 h., cooled, treated with C, and diluted with petr. ether gave 1.03 g. N-PhCH2 derivative (VII) of VI, sparkling white platelets, m. 210° (from aqueous EtOH). VI (0.523 g.) and 7 g. polyphosphoric acid (VIII) heated 2 h. at 150° ($CO_2$ was evolved), and diluted with 50 cc. $H_2O$, and the precipitate sublimed at 200° and 2 mm. gave 0.134 g. I, m. 204-5°; the sublimation residue sublimed at 300° and 2 mm. gave 3,5,7-triphenyl-2,4(1H,3H)-pteridinedione (IX), colorless solid, m. 327-8° (decomposition). III and VIII heated 45 min. at 150° gave 52% I and 63% VII. I (0.97 g.), 2 cc. PhNCO, and 10 cc. pyridine refluxed 3 days, cooled, diluted with 40 cc. $CH_2Cl_2$ and 250 cc. petr. ether, and filtered, and the filtrate evaporated to dryness gave 0.418 g. IX, white needles, m. 327-8° (decomposition) (from aqueous HCONMe2). III gave similarly 51% IX. I (1.52 g.), 3 cc. PhNCS, and 15 cc. pyridine refluxed 1 h., cooled, and diluted with 150 cc. petr. ether yielded 1.92 g. 3-(3-phenylthioureido) analog (X) of I, light yellow platelets, m. 233° (from aqueous HCONMe2). I (1.67 g.), 3 cc. PhNCS, and 15 cc. pyridine refluxed 3 days, cooled overnight, and filtered gave 1.87 g. 2-mercapto-3,6,7-triphenyl-4(3H)-pteridinone (XI), fine yellow needles, m. 301-2° (sublimed at 250° and 1 mm.). X heated similarly with PhNCS gave also XI. N-Bu derivative of I (2.70 g.), 3.5 cc. PhNCS, and 10 cc. pyridine refluxed 4 days, cooled, and diluted with 20 cc. $CH_2Cl_2$ and 100 cc. petr. ether yielded 1.49 g. 2-PhNH analog of XI, pale yellow crystals, m. 323-4° (from aqueous HCONMe2). I (1.34 g.), 2 cc. iso-PrNCS, and 20 cc. pyridine refluxed 2 days, cooled, and diluted with 20 cc. $CHCl_3$ and 100 cc. petr. ether gave 1.05 g. 3-(3-isopropylthioureido) analog (XII) of VI, white platelets, m. 251-2° (from $CH_2Cl_2$-cyclohexane). III (1.04 g.), 1.2 cc. iso-PrNCS, and 15 cc. pyridine refluxed 2 days and poured onto 200 g. ice yielded 0.7 g. N-PhCH2 derivative (XIII) of XII, pale yellow crystals, m. 170° (from 70% AcOH). XII (1.24 g.) refluxed 6 h. with 1 g. Na in 25 cc. absolute EtOH, poured into 100 cc. $H_2O$, and filtered, and the orange solid digested with dilute HCl gave 0.174 g. 2-mercapto-3-isopropyl-6,7-diphenyl-4(3H)-pteridinone, light yellow needles, m. 270° (from aqueous EtOH); the filtrate acidified with concentrated HCl gave 0.72 g. 2-isopropylamino-6,7-diphenyl-4(3H)-pteridinone (XIV), bright lemon-yellow platelets, m. 324-5° (from aqueous EtOH). XIII (0.390 g.) refluxed 3 h. with 0.1 g. Na in 5 cc. absolute EtOH and poured into 50 cc. $H_2O$ yielded 0.30 g. 3-PhCH2 derivative of XIV, sparkling yellow crystals, m. 305-7° (decomposition) (from aqueous HCONMe2). 3-Amino-5,6-diphenylthiopyrazinamide (XV) (1.1 g.) and 10 cc. BzCl refluxed 1.5 h., cooled, diluted with 50 cc. EtOH, refluxed 1 h., and evaporated to dryness, and the residue suspended in hot EtOH and filtered gave 2,6,7-triphenyl-4(3H)-pteridinethione, yellow crystals, m. 323-4° (sublimed). XV (1.23 g.), 3.4 cc. PhNCS, and 10 cc. pyridine refluxed 2 h., cooled, and diluted with 180 cc. petr. ether yielded 2.06 g. compound $C_{47}H_{33}N_9O$ (structure tentatively assigned), fine yellow needles, m. 369-70° (from aqueous HCONMe2), also obtained by refluxing the mixture for 3 days. It was recovered in 93% yield after refluxing 43 h. with concentrated HCl. XV (1.04 g.), 2 cc. PhNCS, and 10 cc. pyridine refluxed 36 h., diluted with 150 cc. hot petr. ether, and allowed to stand gave a small amount of unidentified, colorless needles, m. 72-157°, fine yellow needles, and cushions of orange prisms. The fine yellow needles and orange prisms recrystd. from pyridine-petr. ether yielded 1.15 g. 2-anilino-6,7-diphenyl-4(3H)pteridinethione, long yellow needles, m. 261-2°.

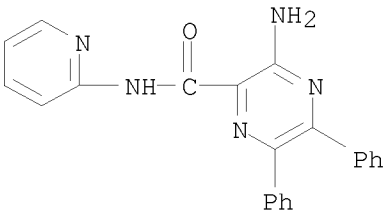
=> d 1-4 hitstr

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
IT 863908-32-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bipyridyl amides as modulators of metabotropic glutamate receptor-5)

RN 863908-32-1 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl-N-2-pyridinyl- (9CI) (CA INDEX NAME)

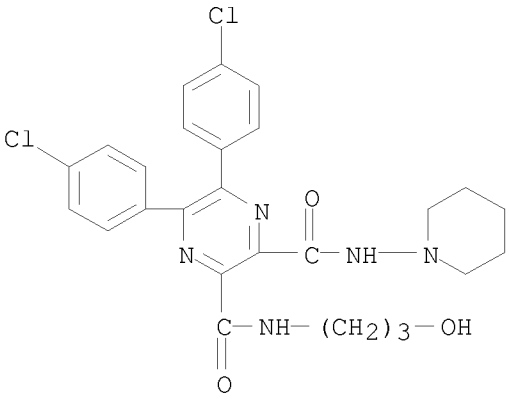


L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

IT 811441-53-9P, 5,6-Bis(4-chlorophenyl)-N-(3-hydroxypropyl)-N'-(piperidin-1-yl)pyrazine-2,3-dicarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 3-substituted 5,6-diarylpyrazine-2-carboxamide and 2-sulfonamide derivs. as CB1 modulators)

RN 811441-53-9 CAPLUS

CN 2,3-Pyrazinedicarboxamide, 5,6-bis(4-chlorophenyl)-N-(3-hydroxypropyl)-N'-1-piperidinyl- (9CI) (CA INDEX NAME)

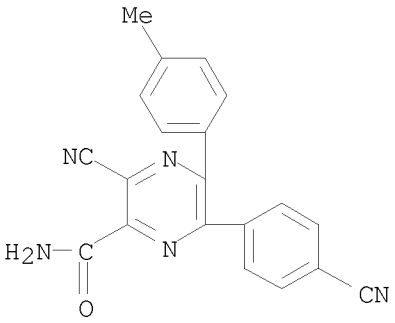


L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

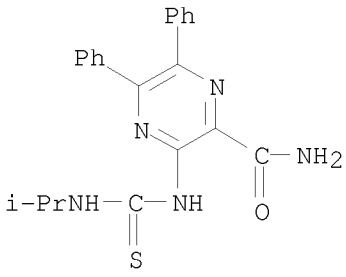
IT 71871-24-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 71871-24-4 CAPLUS

CN Pyrazinecarboxamide, 3-cyano-6-(4-cyanophenyl)-5-(4-methylphenyl)- (9CI) (CA INDEX NAME)




L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
IT 859300-58-6P, Pyrazinamide, 3-(3-isopropyl-2-thioureido)-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)
RN 859300-58-6 CAPLUS
CN Pyrazinamide, 3-(3-isopropyl-2-thioureido)-5,6-diphenyl- (5CI) (CA INDEX NAME)




=> sel 2
E1 THROUGH E16 ASSIGNED

=> s l1 sss full not e1-e16
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 09:51:11 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 6907 TO ITERATE

29.0% PROCESSED 2000 ITERATIONS 4 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 133158 TO 143122
PROJECTED ANSWERS: 53 TO 499

L4 4 SEA SSS SAM L1

L5 4 L4

MISSING OPERATOR L5 SSS
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.47 | 25.82 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | 0.00 | -3.12 |

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FILE COVERS 1907 - 27 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007 (20071226/ED)

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=> file reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.47 | 26.29 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | 0.00 | -3.12 |

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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES:  26 DEC 2007  HIGHEST RN 959588-76-2
DICTIONARY FILE UPDATES:  26 DEC 2007  HIGHEST RN 959588-76-2

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
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predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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FULL SEARCH INITIATED 09:51:36 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  139072 TO ITERATE

100.0% PROCESSED  139072 ITERATIONS                          202 ANSWERS
SEARCH TIME: 00.00.01

L6          202 SEA SSS FUL L1

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
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FULL ESTIMATED COST                              172.10     198.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                0.00      -3.12

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FILE COVERS 1907 - 27 Dec 2007  VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007  (20071226/ED)

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L7          42 L6

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L7 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:84319 CAPLUS
DOCUMENT NUMBER: 146:184452
TITLE: Preparation of thioamides as selective CB1 antagonists for treating obesity, psychiatric and neurol. disorders
INVENTOR(S): Bostrom, Jonas; Cheng, Leifeng; Olsson, Roine
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 44pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007010222 | A2 | 20070125 | WO 2006-GB2638 | 20060717 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2005-14739 A 20050719
OTHER SOURCE(S): CASREACT 146:184452; MARPAT 146:184452
GI

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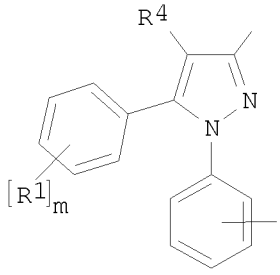

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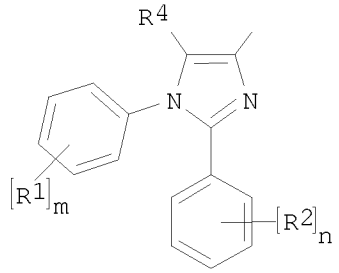

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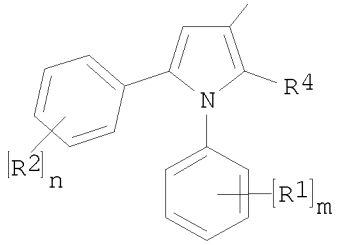
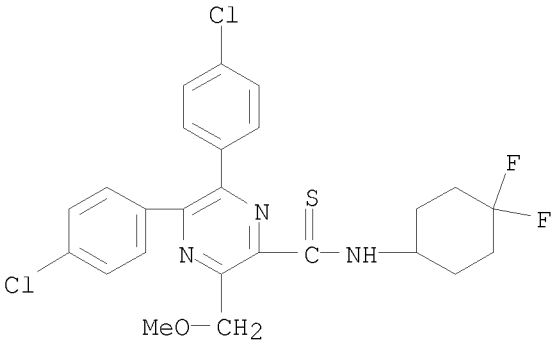


IV

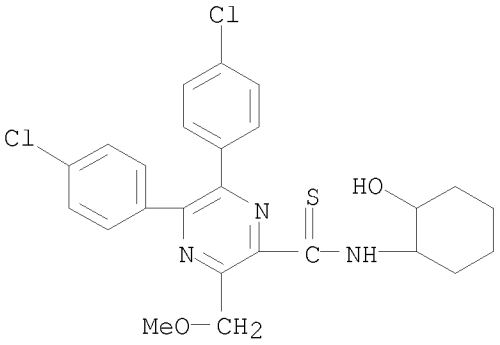
AB The title compds. I [HET = II, III, IV, etc. (wherein R1 = alkoxy (optionally substituted by one or more F atoms), O(CH2)pPh, etc.; p = 1-3; m = 0-3; R2 = alkyl, alkoxy, OH, etc.; n = 0-3; R4 = H, alkyl, alkoxy, etc.); R3 = (un)substituted cyclohexyl, piperidino, Ph, etc.], useful in the treatment of obesity, psychiatric and neurol. disorders, were prepared E.g., a multi-step synthesis of 4-{3-[(cyclohexylamino)carbonothioyl]-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazol-5-yl}phenyl propane-1-sulfonate, starting from 4-hydroxypropiophenone, was given. Compds. I are active at the CB1 receptor (IC50 < 1 μM). The invention also relates to methods for therapeutic use of compds. I and to pharmaceutical compns. containing them.

IT 921628-24-2P 921628-25-3P 921628-26-4P
921628-27-5P 921628-28-6P 921628-29-7P
921628-30-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thioamides as CB1 antagonists for treating obesity, psychiatric and neurol. disorders)

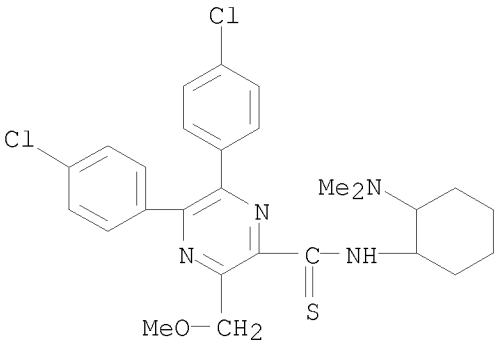
RN 921628-24-2 CAPLUS
CN 2-Pyrazinecarbothioamide, 5,6-bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-(methoxymethyl)- (CA INDEX NAME)



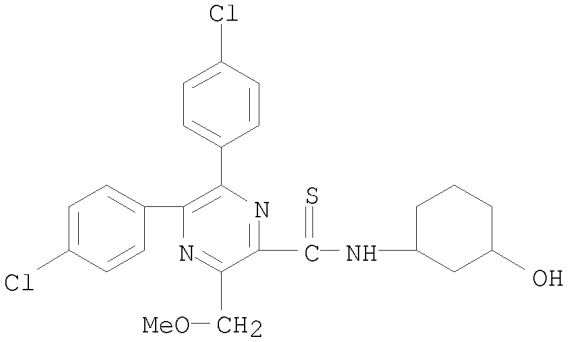

RN 921628-25-3 CAPLUS
CN 2-Pyrazinecarbothioamide, 5,6-bis(4-chlorophenyl)-N-(2-hydroxycyclohexyl)-3-(methoxymethyl)- (CA INDEX NAME)



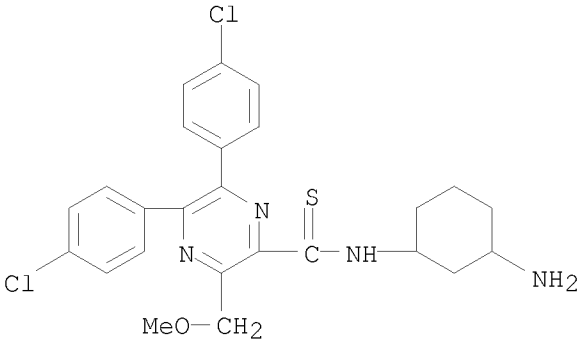

RN 921628-26-4 CAPLUS
CN 2-Pyrazinecarbothioamide, 5,6-bis(4-chlorophenyl)-N-[2-(dimethylamino)cyclohexyl]-3-(methoxymethyl)- (CA INDEX NAME)



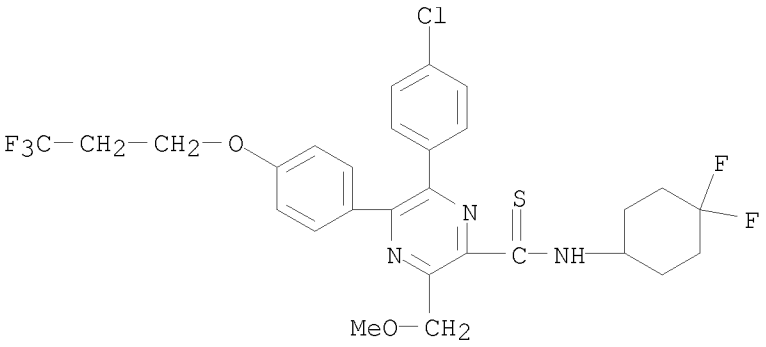

RN 921628-27-5 CAPLUS
CN 2-Pyrazinecarbothioamide, 5,6-bis(4-chlorophenyl)-N-(3-hydroxycyclohexyl)-3-(methoxymethyl)- (CA INDEX NAME)




RN 921628-28-6 CAPLUS
CN 2-Pyrazinecarbothioamide, N-(3-aminocyclohexyl)-5,6-bis(4-chlorophenyl)-3-(methoxymethyl)- (CA INDEX NAME)




RN 921628-29-7 CAPLUS
CN 2-Pyrazinecarbothioamide, 6-(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-(methoxymethyl)-5-[4-(3,3,3-trifluoropropoxy)phenyl]- (CA INDEX NAME)



RN 921628-30-0 CAPLUS
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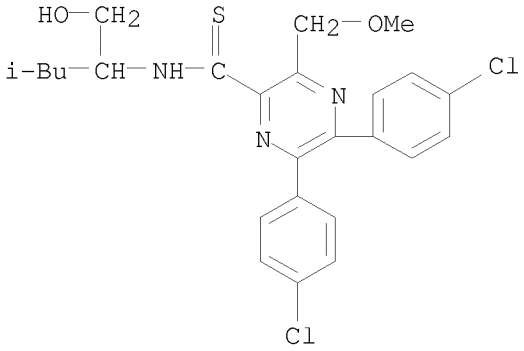


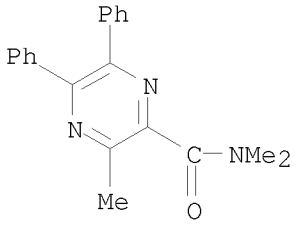
L7 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:646507 CAPLUS
DOCUMENT NUMBER: 145:271733
TITLE: Straightforward Access to Pyrazines, Piperazinones, and Quinoxalines by Reactions of 1,2-Diaza-1,3-butadienes with 1,2-Diamines under Solution, Solvent-Free, or Solid-Phase Conditions
AUTHOR(S): Aparicio, Domitila; Attanasi, Orazio A.; Filippone, Paolino; Ignacio, Roberto; Lillini, Samuele; Mantellini, Fabio; Palacios, Francisco; de Santos, Jesus M.
CORPORATE SOURCE: Istituto di Chimica Organica, Universita degli Studi di Urbino Carlo Bo, Urbino, 61029, Italy
SOURCE: Journal of Organic Chemistry (2006), 71(16), 5897-5905
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:271733
AB The preparation of tetrahydropyrazines, dihydropyrazines, pyrazines, piperazinones, and quinoxalines by 1,4-addition of 1,2-diamines to 1,2-diaza-1,3-butadienes bearing carboxylate, carboxamide, or phosphorylated groups at the terminal carbon and subsequent internal heterocyclization is described. The solvent-free reaction of carboxylated 1,2-diaza-1,3-butadienes with the same reagents affords piperazinones, while phosphorylated 1,2-diaza-1,3-butadienes yield phosphorylated pyrazines. The solid-phase reaction of polymer-bound 1,2-diaza-1,3-

butadienes with 1,2-diamines produces pyrazines.

IT 907161-24-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyrazines, piperazinones, and quinoxalines by 1,4-addition/heterocyclization of 1,2-diaza-1,3-butadienes with 1,2-diamines under solution, solvent-free, or solid-phase conditions)

RN 907161-24-4 CAPLUS

CN Pyrazinecarboxamide, N,N,3-trimethyl-5,6-diphenyl- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1103771 CAPLUS
DOCUMENT NUMBER: 143:367331
TITLE: Pyrazine derivatives as adenosine antagonists, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Tsutsumi, Hideo; Tabuchi, Seiichiro; Minagawa, Masatoshi; Akahane, Atsushi
PATENT ASSIGNEE(S): Astellas Phama Inc., Japan
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005095384 | A1 | 20051013 | WO 2005-JP5663 | 20050322 |
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| CA 2562126 | A1 | 20051013 | CA 2005-2562126 | 20050322 |
| EP 1737841 | A1 | 20070103 | EP 2005-721590 | 20050322 |
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| CN 1938296 | A | 20070328 | CN 2005-80010591 | 20050322 |
| JP 2007530434 | T | 20071101 | JP 2006-529402 | 20050322 |
| IN 2006CN03609 | A | 20070615 | IN 2006-CN3609 | 20060928 |
| MX 2006PA11247 | A | 20061129 | MX 2006-PA11247 | 20060929 |

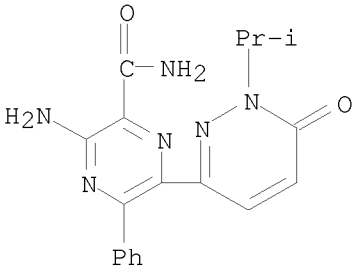
KR 2007008674 A 20070117 KR 2006-722911 20061031
PRIORITY APPLN. INFO.: AU 2004-901772 A 20040401
WO 2005-JP5663 W 20050322
OTHER SOURCE(S): MARPAT 143:367331
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to pyrazine derivs. of formula I, which are adenosine antagonists. In compds. I, R is H or (un)substituted lower alkyl; X is H, halo, OH, SH, cyano, acyl, (un)substituted lower alkyl, (un)substituted lower alkoxy, (un)substituted aryl, etc.; Y is H, halo, OH, SH, cyano, acyl, (un)substituted lower alkyl, (un)substituted lower alkoxy, (un)substituted lower alkylthio, (un)substituted amino, (un)substituted aryl, or (un)substituted heteroaryl; and Z is (un)substituted aryl or (un)substituted heteroaryl; or a salt thereof. The invention also relates to the preparation of I, pharmaceutical compns. containing I, or a pharmaceutically acceptable salt thereof, in admixt. with a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of disorders responding to adenosine antagonists. Oxidation of 2-isopropyl-6-(phenylethynyl)-3-pyridazinone (II) to the corresponding dione followed by condensation with 2,3-diamine-2-butenedinitrile resulted in the formation of pyridazinylpyrazine III, which underwent regioselective substitution with 4-methoxybenzylamine, debenzylation, and hydrolysis to give pyrazinecarboxamide IV. The amide of IV was cleaved followed by decarboxylation, bromination with N-bromosuccinimide, and palladium-catalyzed coupling with 5-ethynyl-1-methyl-1H-imidazole to give pyrazinylpyridazinone V. The tested compds. express high affinity for adenosine receptors, with compound V expressing Ki values of 0.72 nM and 0.25 nM for adenosine A1 and A2a receptors, resp.

IT 866263-05-0P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinecarboxamide 866263-20-9P, 3-Cyano-5-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-6-phenyl-2-pyrazinecarboxamide 866263-29-8P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinecarbothioamide 866264-95-1P, 3-Amino-5-(2-bromophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-2-pyrazinecarboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of pyrazine derivs. as adenosine antagonists)

RN 866263-05-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-phenyl- (9CI) (CA INDEX NAME)

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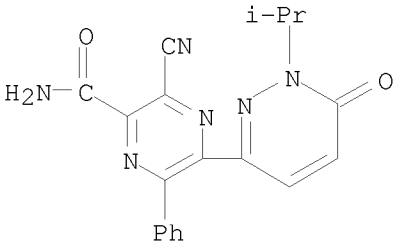

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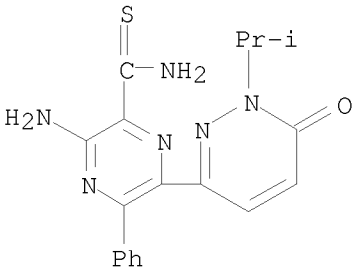

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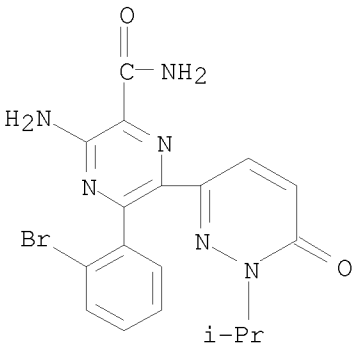

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1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinecarboxamide 866264-96-2P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-(2-thienyl)-2-pyrazinecarboxamide 866264-97-3P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-(4-pyridyl)-2-pyrazinecarboxamide 866264-98-4P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-(6-methoxy-3-pyridyl)-2-pyrazinecarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazine derivs. as adenosine antagonists)

RN 866263-11-8 CAPLUS
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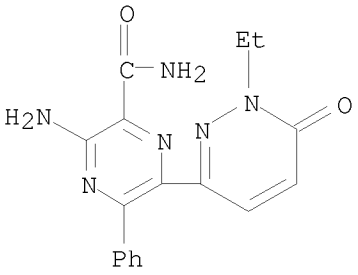

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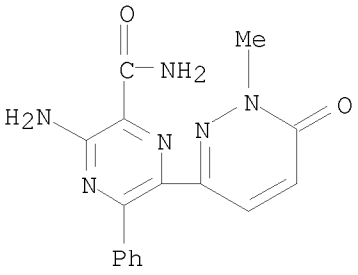

RN 866263-21-0 CAPLUS
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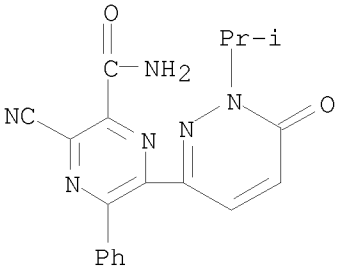

RN 866263-33-4 CAPLUS

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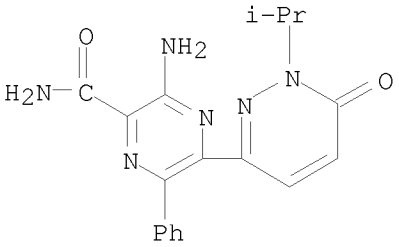

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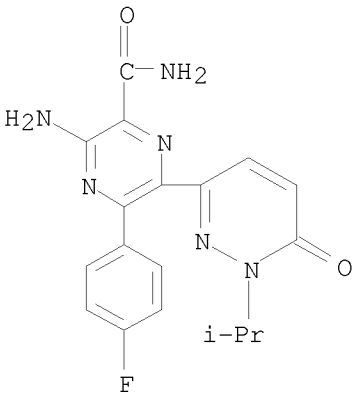

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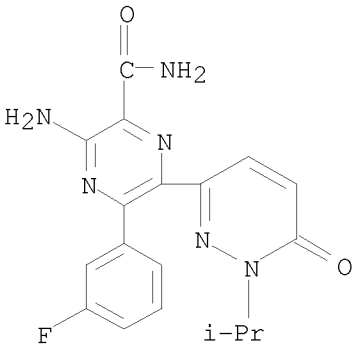

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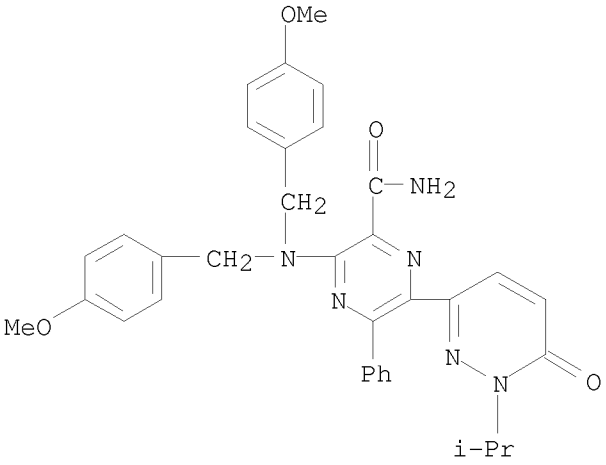


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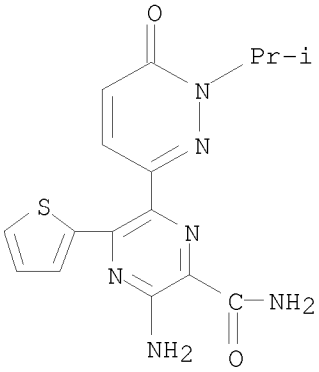


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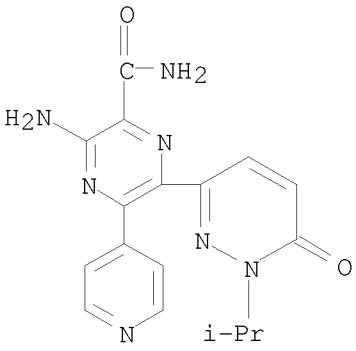


RN 866264-98-4 CAPLUS
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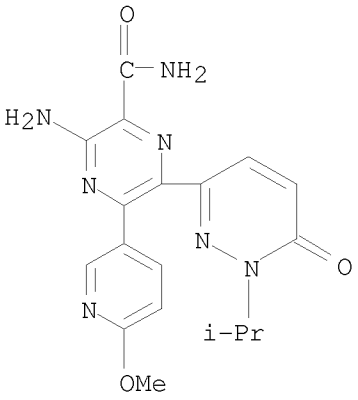

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1078246 CAPLUS
DOCUMENT NUMBER: 143:367330
TITLE: Pyrazine derivatives as adenosine antagonists, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Tsutsumi, Hideo; Tabuchi, Seiichiro; Minagawa, Masatoshi; Akahane, Atsushi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 54 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005222159 | A1 | 20051006 | US 2005-87761 | 20050324 |
| US 7265120 | B2 | 20070904 | | |
| PRIORITY APPLN. INFO.: | | | AU 2004-901772 A | 20040401 |
| OTHER SOURCE(S): | MARPAT 143:367330 | | | |

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AB The invention relates to pyrazine derivs. of formula I, which are adenosine antagonists. In compds. I, R is H or (un)substituted lower alkyl; X is H, halo, OH, SH, cyano, acyl, (un)substituted lower alkyl, (un)substituted lower alkoxy, (un)substituted aryl, etc.; Y is H, halo, OH, SH, cyano, acyl, (un)substituted lower alkyl, (un)substituted lower alkoxy, (un)substituted lower alkylthio, (un)substituted amino, (un)substituted aryl, or (un)substituted heteroaryl; and Z is (un)substituted aryl or (un)substituted heteroaryl; or a salt thereof. The invention also relates to the preparation of I, pharmaceutical compns. containing I, or a pharmaceutically acceptable salt thereof, in admixt. with a pharmaceutically acceptable carrier, as well as to the use of the compns. in the treatment of disorders responding to adenosine antagonists. Oxidation of 2-isopropyl-6-(phenylethynyl)-3-pyridazinone (II) to the corresponding

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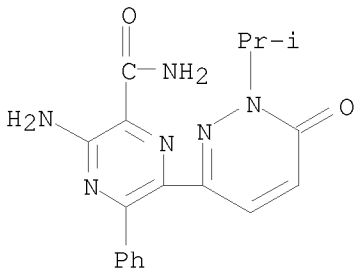

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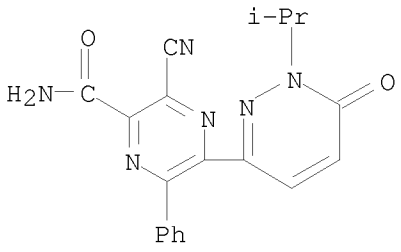

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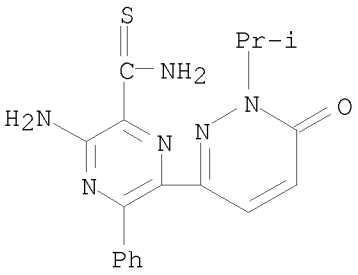


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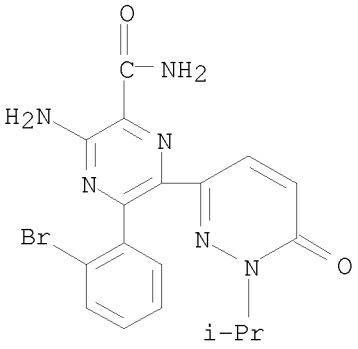


IT 866263-11-8P, 3-Amino-6-(1-ethyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinecarboxamide 866263-15-2P, 3-Amino-6-(1-methyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinecarboxamide 866263-21-0P, 3-Cyano-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinecarboxamide 866263-33-4P, 3-Amino-5-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-6-phenyl-2-pyrazinecarboxamide 866263-45-8P, 3-Amino-5-(4-fluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-2-pyrazinecarboxamide 866263-47-0P 866263-55-0P, 3-[Bis(4-methoxybenzyl)amino]-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-phenyl-2-pyrazinecarboxamide 866264-96-2P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-(2-thienyl)-2-pyrazinecarboxamide 866264-97-3P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-(4-pyridyl)-2-pyrazinecarboxamide 866264-98-4P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridazinyl)-5-(6-methoxy-3-pyridyl)-2-pyrazinecarboxamide
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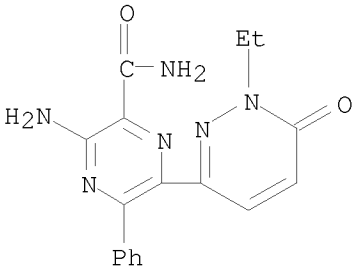

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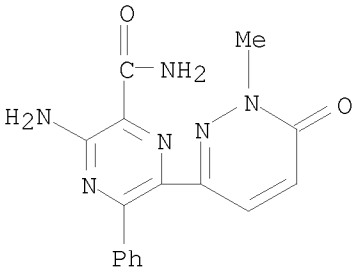

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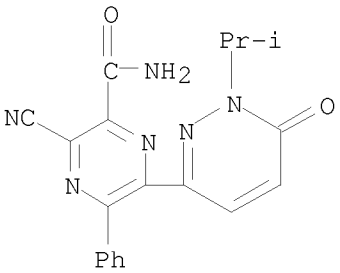

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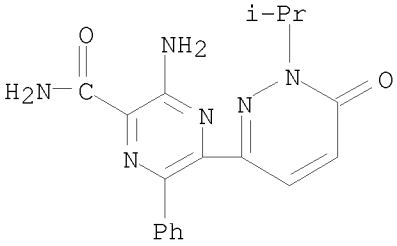
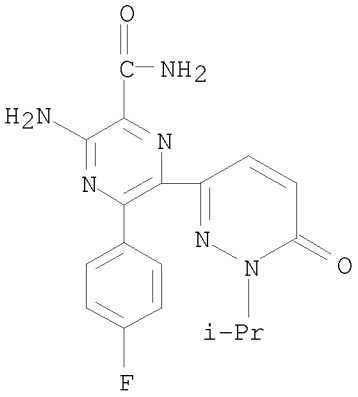
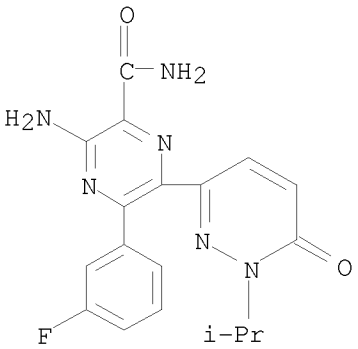


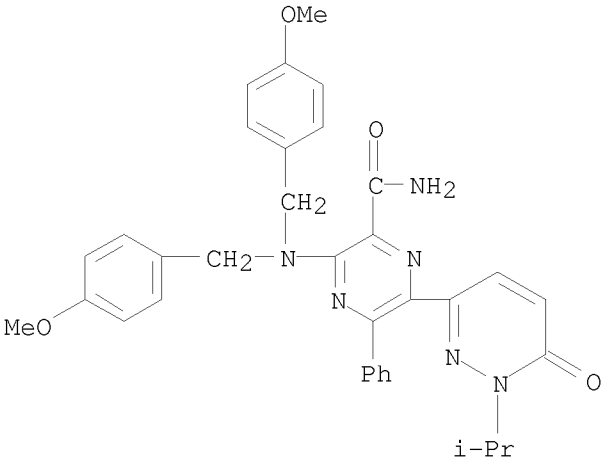
RN 866263-45-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



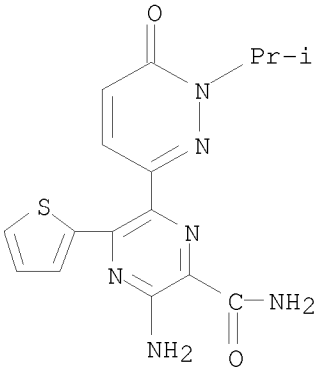
RN 866263-47-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-(3-fluorophenyl)- (9CI) (CA INDEX NAME)



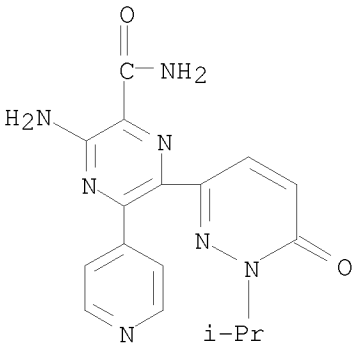
RN 866263-55-0 CAPLUS
CN Pyrazinecarboxamide, 3-[bis[(4-methoxyphenyl)methyl]amino]-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-phenyl- (9CI) (CA INDEX NAME)



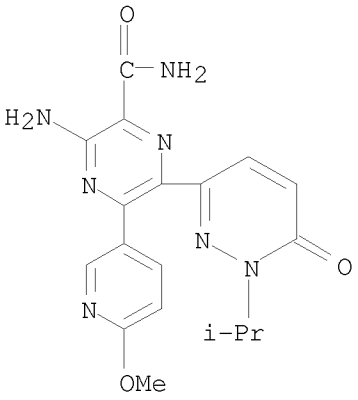

RN 866264-96-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-(2-thienyl)- (9CI) (CA INDEX NAME)




RN 866264-97-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



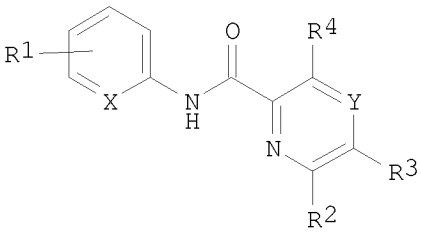

RN 866264-98-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridazinyl]-5-(6-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)




L7 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:962046 CAPLUS
DOCUMENT NUMBER: 143:266952
TITLE: Preparation of bipyridyl amides as modulators of metabotropic glutamate receptor-5
INVENTOR(S): Bonnefous, Celine; Kamenecka, Theodore M.; Vernier, Jean-Michel
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2005079802 | A1 | 20050901 | WO 2005-US3952 | | 20050209 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| AU 2005215379 | A1 | 20050901 | AU 2005-215379 | | 20050209 |
| CA 2555402 | A1 | 20050901 | CA 2005-2555402 | | 20050209 |
| EP 1715867 | A1 | 20061102 | EP 2005-713111 | | 20050209 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS | | | | | |
| CN 1933838 | A | 20070321 | CN 2005-80004732 | | 20050209 |
| JP 2007524682 | T | 20070830 | JP 2006-553189 | | 20050209 |
| IN 2006DN04346 | A | 20070713 | IN 2006-DN4346 | | 20060727 |
| US 2007149547 | A1 | 20070628 | US 2006-589407 | | 20060811 |
| PRIORITY APPLN. INFO.: | | | US 2004-544627P | P | 20040212 |
| | | | WO 2005-US3952 | W | 20050209 |

OTHER SOURCE(S): CASREACT 143:266952; MARPAT 143:266952
GI



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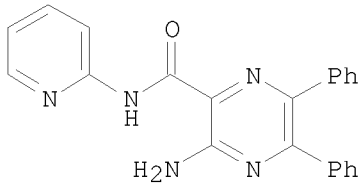


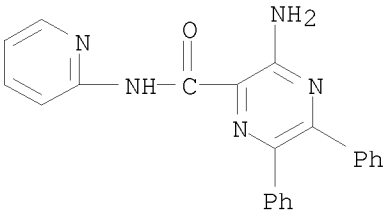
II

AB The title compds. I [X = N, C; Y = N, C, C(halo); R1 = H, alkyl, cycloalkyl, etc.; R2 = H, alkyl, aryl, etc.; R3 = aryl, halo, alkyl, etc.; R2 and R3 may be joined together with the atoms to which they are attached to form a (un)saturated 4-7 membered ring containing 0-2 heteroatoms selected from O, S and N; R4 = aryl, heteroaryl, halo, etc.] which are mGluR5 modulators useful in the treatment or prevention of diseases and conditions in which mGluR5 is involved, including but not limited to psychiatric and mood disorders such as schizophrenia, anxiety, depression, bipolar disorders, and panic, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm and sleep disorders, such as shift-work induced sleep disorder and jet-lag, drug addiction, drug abuse, drug withdrawal, obesity and other diseases, were prepared Thus, amidation of pyridin-2-amine with 3-amino-5,6-diphenylpyrazine-2-carboxylic acid afforded the amide II. The exemplified compds. I have mGluR5 inhibitory activity as shown by inhibition at 10 μM or less in the calcium flux assay or 100 μM or less or less in the PI assay. The invention is also directed to pharmaceutical compns. comprising compds. I.

IT 863908-32-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bipyridyl amides as modulators of metabotropic glutamate receptor-5)

RN 863908-32-1 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl-N-2-pyridinyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:493608 CAPLUS
DOCUMENT NUMBER: 143:43904
TITLE: Preparation of pyrrolo[3,4-b]pyrazine-5,7(6H)-dione derivatives for treating obesity, psychiatric, and neurological disorders
INVENTOR(S): Cheng, Leifeng
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

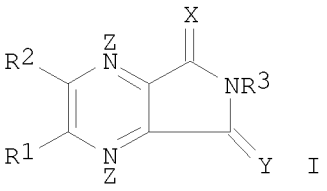
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005051953 | A2 | 20050609 | WO 2004-GB4934 | 20041124 |
| WO 2005051953 | A3 | 20050728 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004292493 | A1 | 20050609 | AU 2004-292493 | 20041124 |
| CA 2546318 | A1 | 20050609 | CA 2004-2546318 | 20041124 |
| EP 1701958 | A2 | 20060920 | EP 2004-798641 | 20041124 |
| EP 1701958 | B1 | 20070502 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS | | | | |
| CN 1886405 | A | 20061227 | CN 2004-80034802 | 20041124 |
| AT 361301 | T | 20070515 | AT 2004-798641 | 20041124 |
| JP 2007512298 | T | 20070517 | JP 2006-540602 | 20041124 |
| ES 2285544 | T3 | 20071116 | ES 2004-4798641 | 20041124 |
| IN 2006DN02621 | A | 20070824 | IN 2006-DN2621 | 20060510 |
| US 2007099923 | A1 | 20070503 | US 2006-579830 | 20060517 |
| HK 1096670 | A1 | 20071012 | HK 2007-101236 | 20070201 |

PRIORITY APPLN. INFO.: GB 2003-27331 A 20031125

WO 2004-GB4934 W 20041124

OTHER SOURCE(S): CASREACT 143:43904; MARPAT 143:43904

GI

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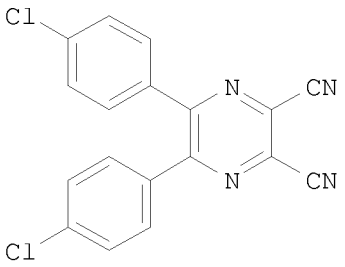
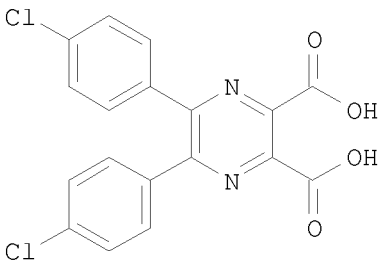



II

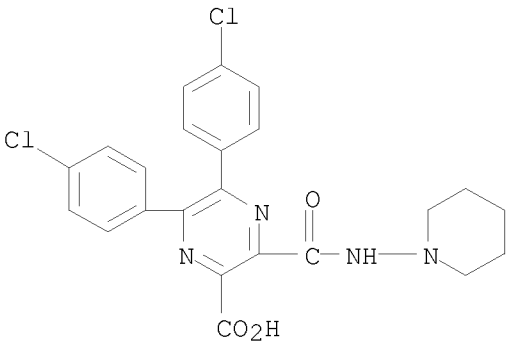



III

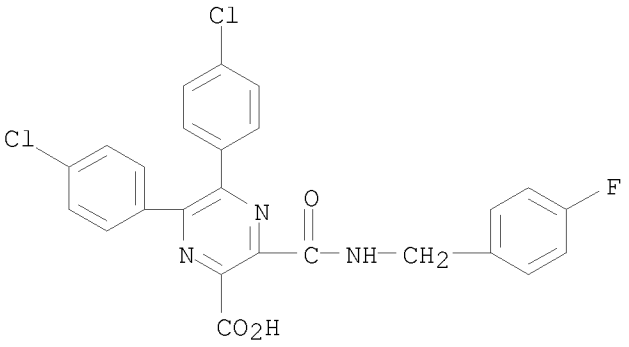
AB The title compds. I [R1, R2 = Ph, thienyl, pyridyl, C1-C10-alkyl, C1-C10-alkoxy, C3-C15-cycloalkyl; R3 = C1-C15-alkyl, C3-C15-cycloalkyl, phenylC1-C4-alkyl, heteroaryl, heteroarylC1-C4-alkyl, R4(CH2)n, R4 = heterocycle, n = 0-4; X, Y = O, S; Z = (O)n, n = 0, 1] were prepared and are designed to be used in the treatment of obesity, psychiatric disorders, neurol. disorders, immune, cardiovascular, reproductive, and endocrine disorders, septic shock, diseases related to respiratory and gastrointestinal systems, and extended abuse, addiction and/or relapse indications. As an example, 1,2-bis(4-chlorophenyl)ethane-1,2-dione reacted with diaminomaleonitrile to give pyrazine-2,3-dicarbonitrile II which was treated with KOH/H2O2 in H2O, esterified, and hydrolyzed to give dicarboxylic acid III. III condensed with 4-FC6H4CH2NH2 to give the mono-amide which cyclized to give the desired compound I (R1 = R2 = 4-ClC6H4, R3 = 4-FC6H4CH2, X = Y = O, Z = none).

IT 811441-51-7P, 5,6-Bis(4-chlorophenyl)-3-[(piperidin-1-ylamino)carbonyl]pyrazine-2-carboxylic acid 853578-19-5P 853578-23-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrrolo[3,4-b]pyrazine-5,7(6H)-dione derivs. for treating obesity, psychiatric, neurol., immune, cardiovascular, reproductive, and endocrine disorders, septic shock, respiratory and gastrointestinal disorders)

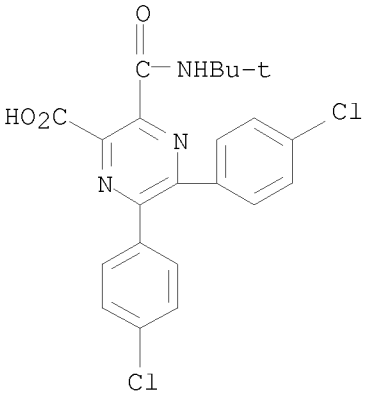
RN 811441-51-7 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]- (9CI) (CA INDEX NAME)




RN 853578-19-5 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[[(4-fluorophenyl)methyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



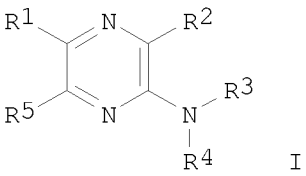
RN 853578-23-1 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(1,1-dimethylethyl)amino]carbonyl]- (9CI) (CA INDEX NAME)



L7 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:450934 CAPLUS
DOCUMENT NUMBER: 143:7731
TITLE: Preparation of pyrazine derivatives as adenosine receptor antagonists for treating neurological, cardiovascular, and other diseases
INVENTOR(S): Yonishi, Satoshi; Aoki, Satoshi; Matsushima, Yuji; Akahane, Atsushi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co. Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2005113387 | A1 | 20050526 | US 2004-972340 | | 20041026 |
| PRIORITY APPLN. INFO.: | | | EP 2003-905895 | A | 20031027 |
| | | | EP 2004-902764 | A | 20040524 |

OTHER SOURCE(S): MARPAT 143:7731
GI



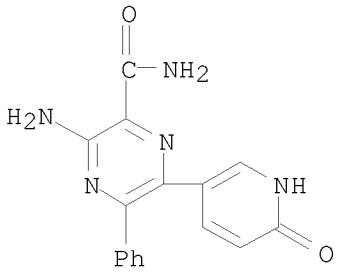
I

AB Pyrazine derivative of formula I (with variables defined below) or salts thereof are claimed. The pyrazine compound I are adenosine antagonists and are useful for the prevention and/or treatment of depression, dementia (e.g. Alzheimer's disease, cerebrovascular dementia, dementia accompanying Parkinson's disease, etc.), Parkinson's disease, anxiety, pain,

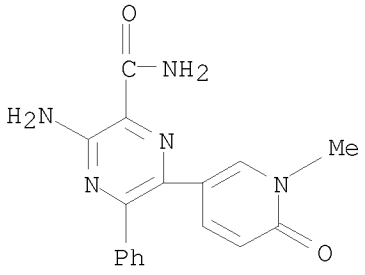
cerebrovascular disease (e.g. stroke, etc.), heart failure and the like. A process for preparing the pyrazines and pharmaceutical compns. containing them are also claimed. For I, R1 is substituted pyridin-2-one or pyridine; R2 is H, OH, halogen, cyano, or optionally substituted lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, aryloxy, arylthio, acyl, aryl, heterocyclic group or amino; R3 and R4 are independently H, lower alkyl or acyl; and R5 is optionally substituted lower alkyl, lower alkenyl, lower alkynyl, cyano, aryl or heterocyclic group.

IT 851087-21-3P, 3-Amino-6-(6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-22-4P, 3-Amino-6-(1-methyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-39-3P, 3-Amino-5-(4-fluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-45-1P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(4-methoxyphenyl)-2-pyrazinecarboxamide 851087-73-5P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-N-methoxy-N-methyl-5-phenyl-2-pyrazinecarboxamide 851087-95-1P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(2-pyridyl)-2-pyrazinecarboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of pyrazine derivs. as adenosine receptor antagonists for treating neurol., cardiovascular, and other diseases)

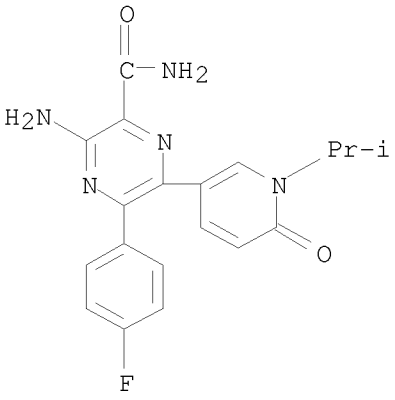
RN 851087-21-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-6-oxo-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



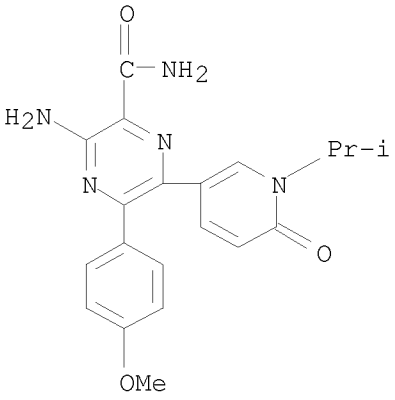
RN 851087-22-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



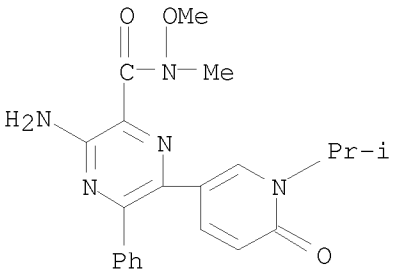
RN 851087-39-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



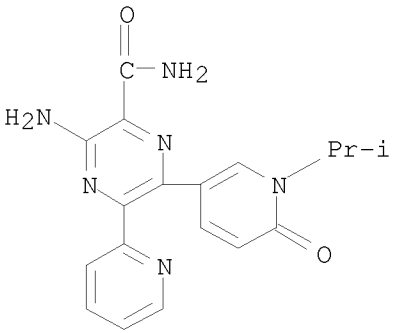
RN 851087-45-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



RN 851087-73-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-methoxy-N-methyl-5-phenyl- (9CI) (CA INDEX NAME)



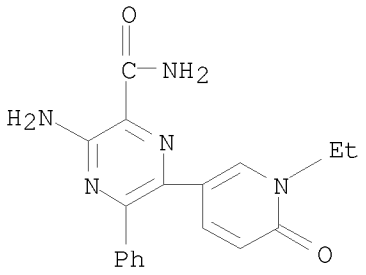
RN 851087-95-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



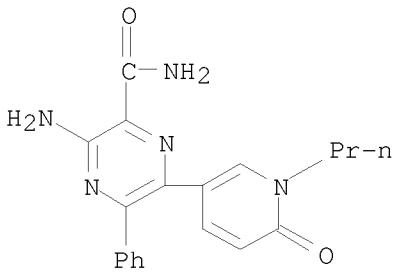
IT 851087-23-5P, 3-Amino-6-(1-ethyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-24-6P, 3-Amino-6-(6-oxo-1-propyl-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-25-7P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-26-8P, 3-Amino-6-(6-isopropoxy-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-36-0P, 3-Amino-6-(6-methoxy-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-37-1P, 3-Amino-5-(2-fluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-38-2P, 3-Amino-5-(3-fluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-40-6P, 3-Amino-5-(2-chlorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-41-7P, 3-Amino-5-(3-chlorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-42-8P, 3-Amino-5-(4-chlorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-43-9P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(2-methoxyphenyl)-2-pyrazinecarboxamide 851087-44-0P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(3-methoxyphenyl)-2-pyrazinecarboxamide 851087-46-2P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-[2-(trifluoromethoxy)phenyl]-2-pyrazinecarboxamide 851087-47-3P , 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-[3-(trifluoromethoxy)phenyl]-2-pyrazinecarboxamide 851087-48-4P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-[4-(trifluoromethoxy)phenyl]-2-pyrazinecarboxamide 851087-49-5P, 3-Amino-5-(3,4-difluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-50-8P, 3-Amino-5-(3,5-difluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-51-9P, 3-Amino-5-(4-cyanophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-62-2P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-N-methyl-5-phenyl-2-pyrazinecarboxamide 851087-63-3P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-N,N-dimethyl-5-phenyl-2-pyrazinecarboxamide 851087-65-5P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-N-[(2-pyridyl)methyl]-2-pyrazinecarboxamide 851087-66-6P, 3-Amino-N-(cyanomethyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-69-9P, 3-Amino-N-(2-hydroxyethyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-70-2P, 3-Amino-N-cyclopropyl-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-77-9P, 3-Amino-N-[2-(dimethylamino)ethyl]-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-78-0P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(2-methylphenyl)-2-pyrazinecarboxamide 851087-79-1P, 3-Amino-5-(2,3-difluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-80-4P, 3-Amino-5-(2,4-difluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-

2-pyrazinecarboxamide 851087-81-5P, 3-Amino-5-(2,5-difluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-82-6P, 3-Amino-5-(2-furyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-83-7P, 3-Amino-5-(3-furyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-84-8P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(2-thienyl)-2-pyrazinecarboxamide 851087-85-9P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(3-thienyl)-2-pyrazinecarboxamide 851087-86-0P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(5-methyl-2-thienyl)-2-pyrazinecarboxamide 851087-87-1P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(1H-pyrazol-4-yl)-2-pyrazinecarboxamide 851087-89-3P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(3-pyridyl)-2-pyrazinecarboxamide 851087-90-6P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(4-pyridyl)-2-pyrazinecarboxamide 851087-91-7P, 3-Amino-5-(4-fluorophenyl)-6-(1-methyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-92-8P, 3-Amino-5-(2-furyl)-6-(1-methyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-93-9P, 3-Amino-6-(1-methyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(2-thienyl)-2-pyrazinecarboxamide 851088-51-2P, 3-Amino-5-(4-fluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-N-methyl-2-pyrazinecarboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazine derivs. as adenosine receptor antagonists for treating neurol., cardiovascular, and other diseases)

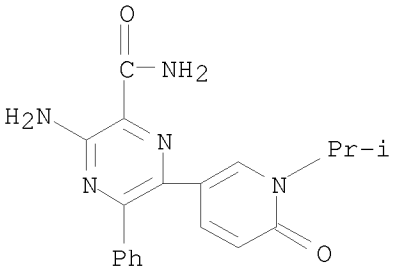
RN 851087-23-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1-ethyl-1,6-dihydro-6-oxo-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



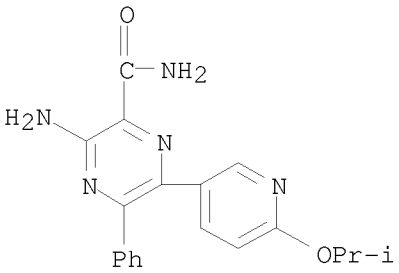

RN 851087-24-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-6-oxo-1-propyl-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



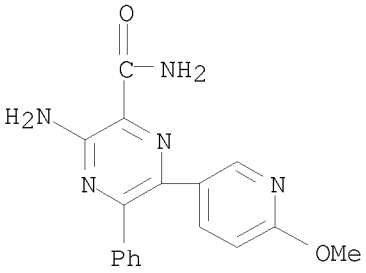
RN 851087-25-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



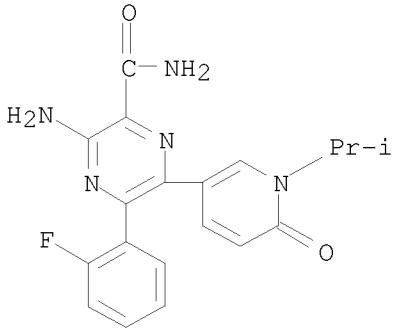
RN 851087-26-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[6-(1-methylethoxy)-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



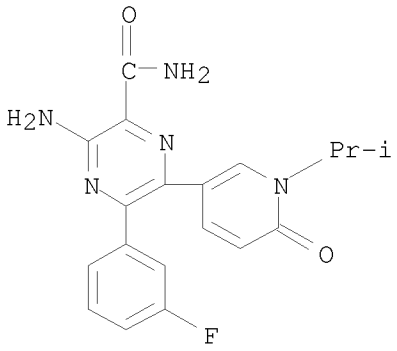
RN 851087-36-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(6-methoxy-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



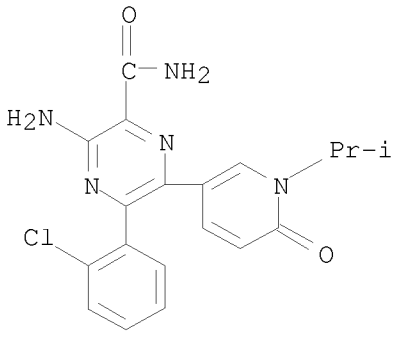
RN 851087-37-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



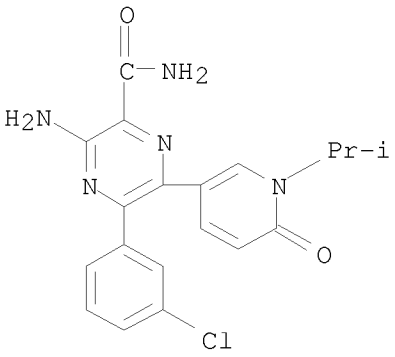
RN 851087-38-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-fluorophenyl)- (9CI) (CA INDEX NAME)



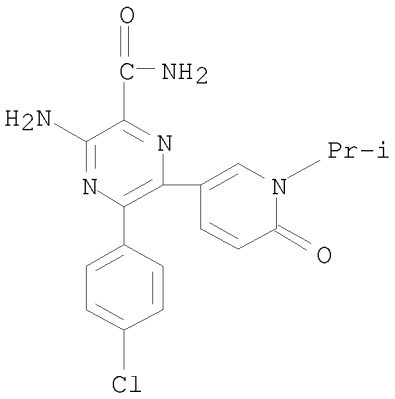
RN 851087-40-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2-chlorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



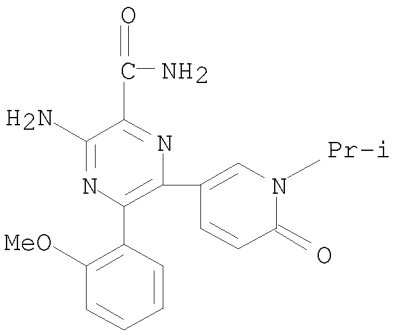
RN 851087-41-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(3-chlorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



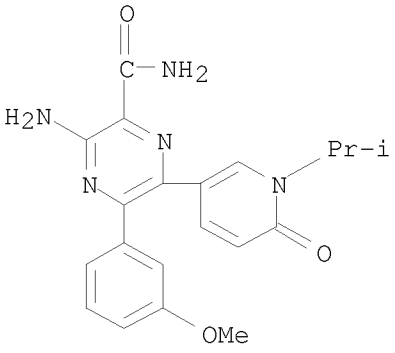
RN 851087-42-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(4-chlorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



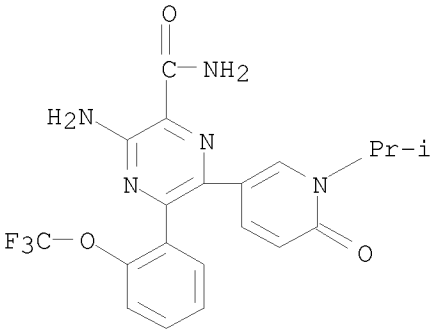
RN 851087-43-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



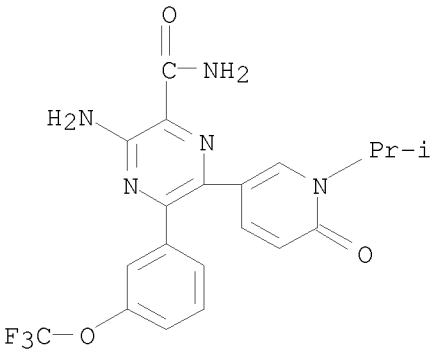
RN 851087-44-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



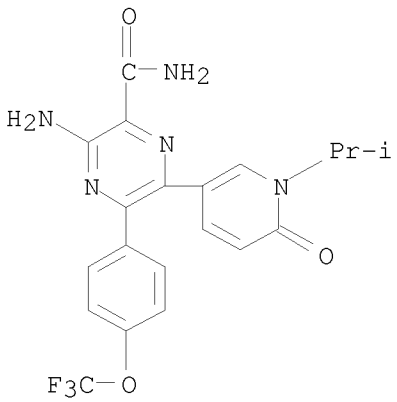
RN 851087-46-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-[2-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



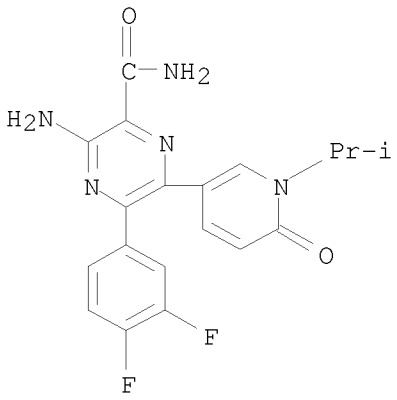
RN 851087-47-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-[3-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



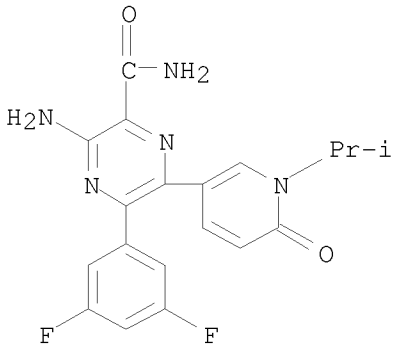
RN 851087-48-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



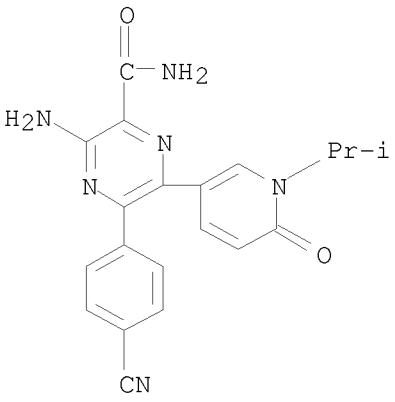
RN 851087-49-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(3,4-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



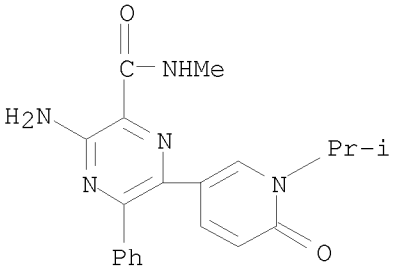
RN 851087-50-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(3,5-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



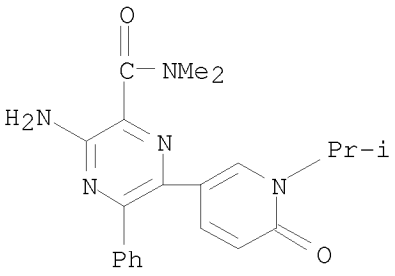
RN 851087-51-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(4-cyanophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



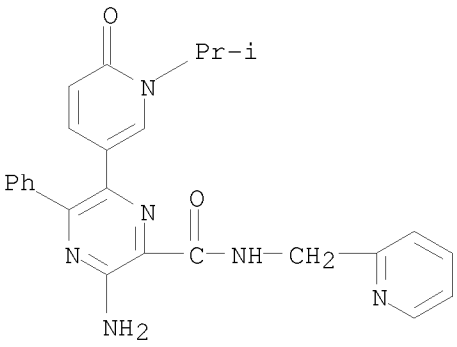
RN 851087-62-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-methyl-5-phenyl- (9CI) (CA INDEX NAME)



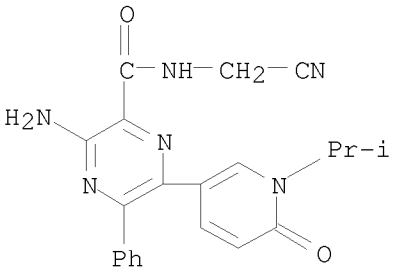
RN 851087-63-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N,N-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



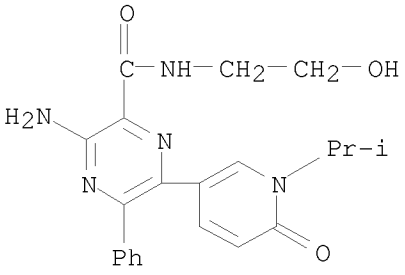
RN 851087-65-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl-N-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



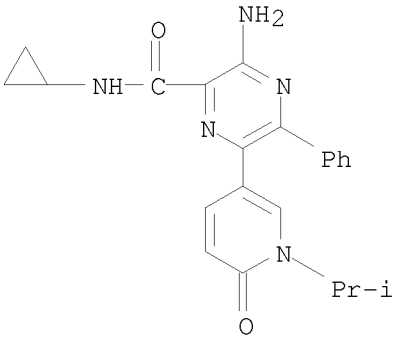
RN 851087-66-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(cyanomethyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



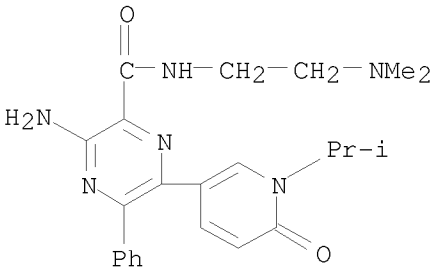
RN 851087-69-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-(2-hydroxyethyl)-5-phenyl- (9CI) (CA INDEX NAME)



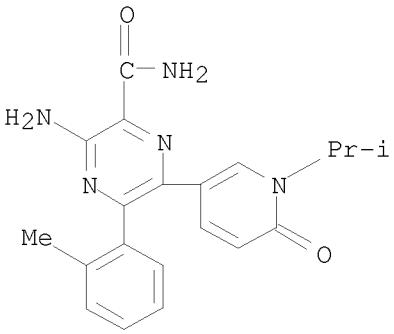
RN 851087-70-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-cyclopropyl-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



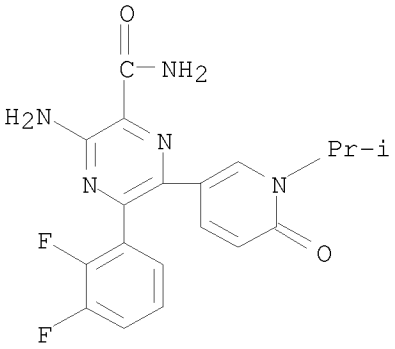
RN 851087-77-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-[2-(dimethylamino)ethyl]-5-phenyl- (9CI) (CA INDEX NAME)



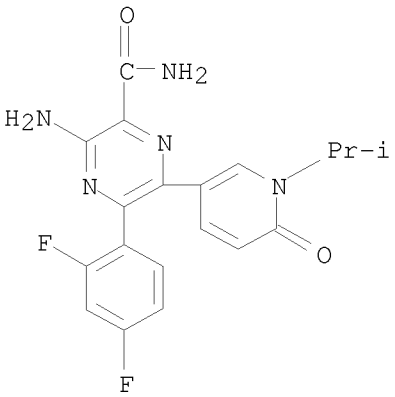
RN 851087-78-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-methylphenyl)- (9CI) (CA INDEX NAME)



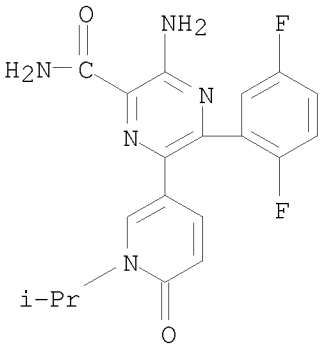
RN 851087-79-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2,3-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



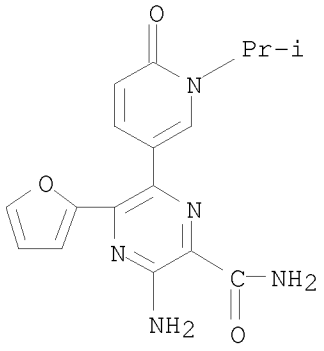
RN 851087-80-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2,4-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



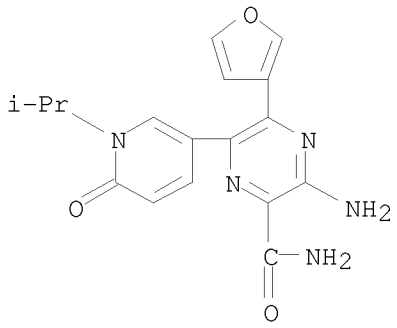
RN 851087-81-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2,5-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



RN 851087-82-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-furanyl)- (9CI) (CA INDEX NAME)



RN 851087-83-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-furanyl)- (9CI) (CA INDEX NAME)



RN 851087-84-8 CAPLUS
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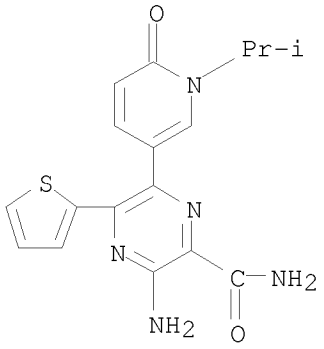

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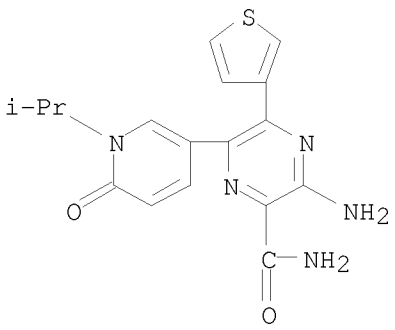
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-thienyl)- (9CI) (CA INDEX NAME)



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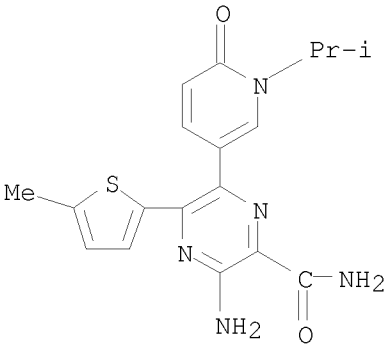
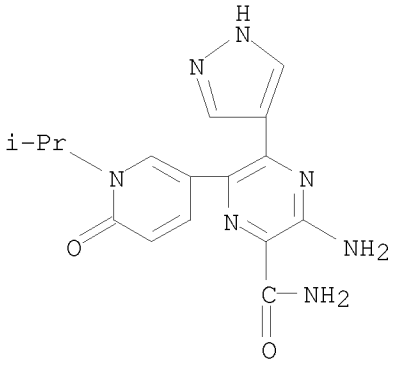
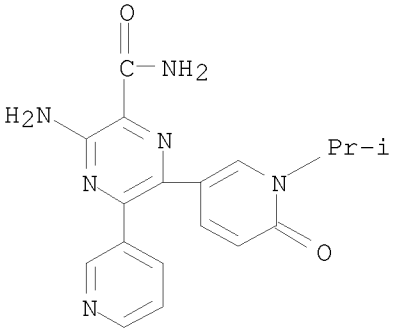
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(5-methyl-2-thienyl)- (9CI) (CA INDEX NAME)



RN 851087-87-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



RN 851087-89-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-pyridinyl)- (9CI) (CA INDEX NAME)



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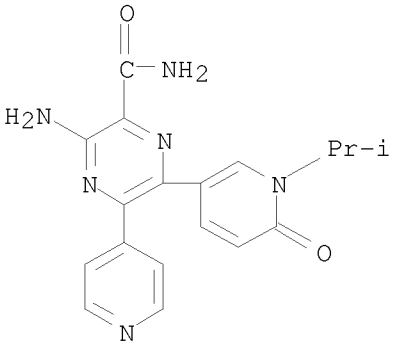

RN 851087-91-7 CAPLUS
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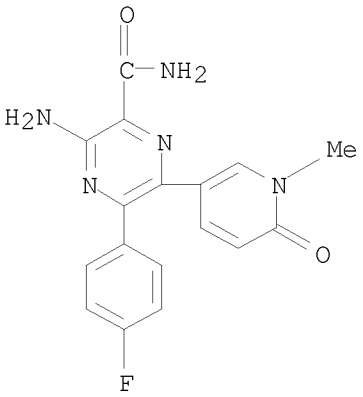

RN 851087-92-8 CAPLUS
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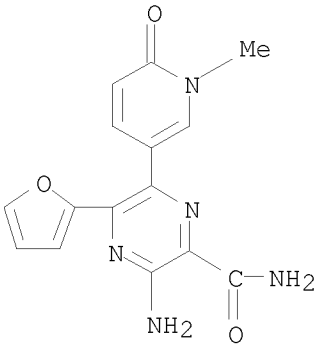

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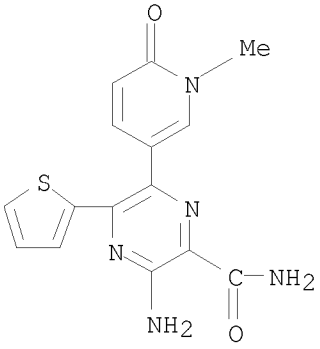
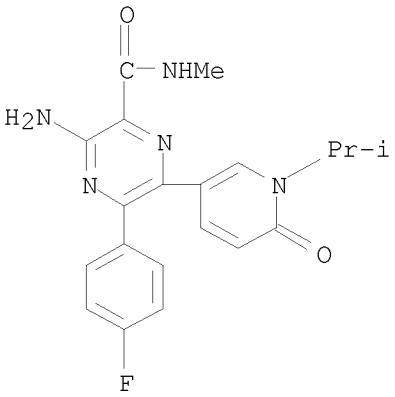
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-5-(2-thienyl)- (9CI) (CA INDEX NAME)



RN 851088-51-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(4-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



L7 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:395298 CAPLUS
DOCUMENT NUMBER: 142:447235
TITLE: Preparation of pyrazines as adenosine A1 and A2a receptor antagonists and their pharmaceutical compositions

INVENTOR(S): Yonishi, Satoshi; Aoki, Satoshi; Matsushima, Yuji; Akahane, Atsushi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2005040151 | A1 | 20050506 | WO 2004-JP16193 | | 20041025 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
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| AU 2004283990 | A1 | 20050506 | AU 2004-283990 | | 20041025 |
| CA 2543644 | A1 | 20050506 | CA 2004-2543644 | | 20041025 |
| EP 1678160 | A1 | 20060712 | EP 2004-793294 | | 20041025 |
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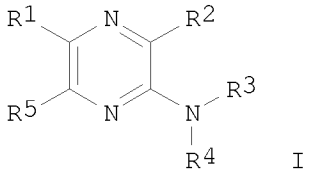
| CN 1871231 | A | 20061129 | CN 2004-80031570 | | 20041025 |
| BR 2004015863 | A | 20070109 | BR 2004-15863 | | 20041025 |
| JP 2007510620 | T | 20070426 | JP 2006-519017 | | 20041025 |
| MX 2006PA04575 | A | 20061120 | MX 2006-PA4575 | | 20060425 |
| NO 2006002303 | A | 20060719 | NO 2006-2303 | | 20060522 |
| PRIORITY APPLN. INFO.: | | | AU 2003-905895 | A | 20031027 |
| | | | AU 2004-902764 | A | 20040524 |
| | | | WO 2004-JP16193 | W | 20041025 |

OTHER SOURCE(S): CASREACT 142:447235; MARPAT 142:447235

GI



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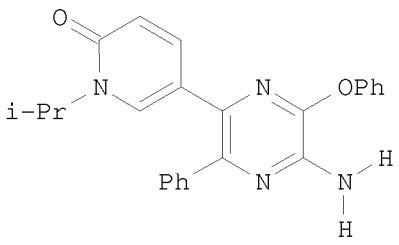


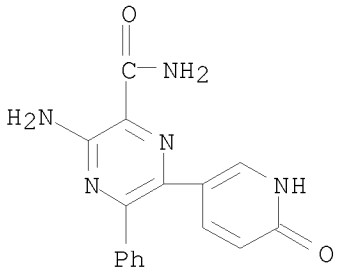
II

AB Title compound I [wherein R1 = N,3-disubstituted 2(1H)-pyridinonyl, 2-alkoxypyridinyl; R2 = H, OH, halo, CN, (un)substituted lower alk(en/yn)yl, alkoxy, aryloxy, arylthio, acyl, aryl, heterocyclyl or amino; R3, R4 = independently H, lower alkyl, acyl; and their salts] and their salts were prepared as adenosine receptor antagonists. For example, compound II was prepared by etherification of 5-(5-Amino-6-bromo-3-phenyl-2-pyrazinyl)-1-isopropyl-2(1H)-pyridinone (preparation given) with phenol. II showed binding to the human A1 adenosine receptor with Ki = 1.57 nM and to the human A2a adenosine receptor with Ki = 0.32 nM. Thus, I are useful as A1 receptor and A2a receptor dual antagonists and for the prevention and/or treatment of depression, dementia (e.g. Alzheimer's disease, cerebrovascular dementia, dementia accompanying Parkinson's disease, etc.), Parkinson's disease, anxiety, pain, cerebrovascular disease (e.g. stroke, etc.), heart failure and the like (no data).

IT 851087-21-3P, 3-Amino-6-(6-oxo-1,6-dihydro-3-pyridyl)-5-phenyl-2-pyrazinecarboxamide 851087-39-3P, 3-Amino-5-(4-fluorophenyl)-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-2-pyrazinecarboxamide 851087-45-1P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(4-methoxyphenyl)-2-pyrazinecarboxamide 851087-73-5P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-N-methoxy-N-methyl-5-phenyl-2-pyrazinecarboxamide 851087-95-1P, 3-Amino-6-(1-isopropyl-6-oxo-1,6-dihydro-3-pyridyl)-5-(2-pyridyl)-2-pyrazinecarboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of pyrazines as adenosine receptor antagonists)

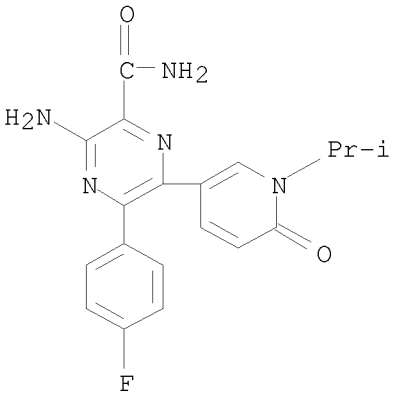
RN 851087-21-3 CAPLUS

CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-6-oxo-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)




RN 851087-39-3 CAPLUS

CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 851087-45-1 CAPLUS
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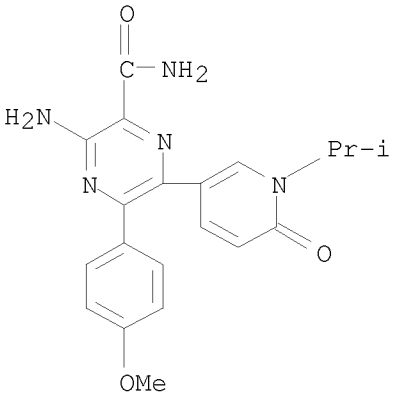
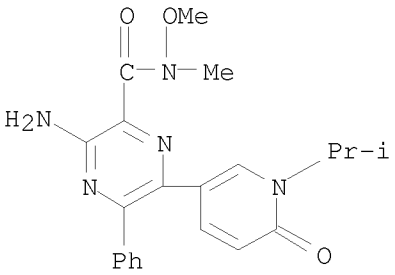
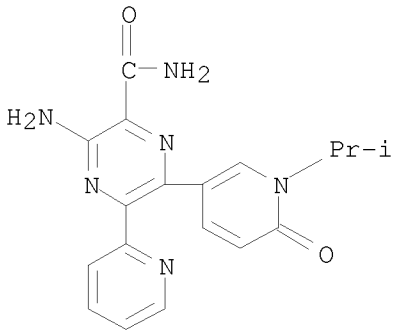


RN 851087-73-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-methoxy-N-methyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 851087-95-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)



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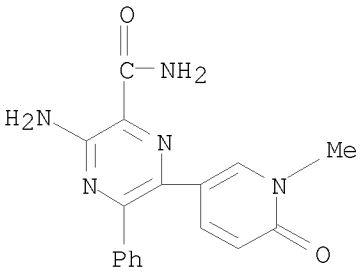
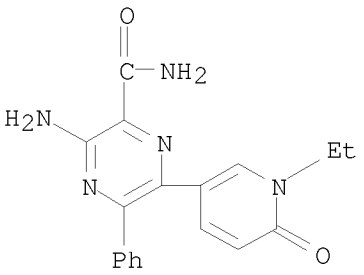
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrazines as adenosine receptor antagonists)

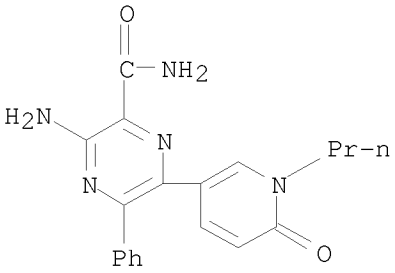
RN 851087-22-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



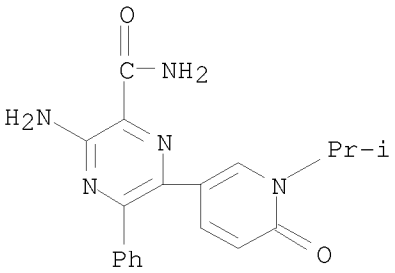

RN 851087-23-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1-ethyl-1,6-dihydro-6-oxo-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



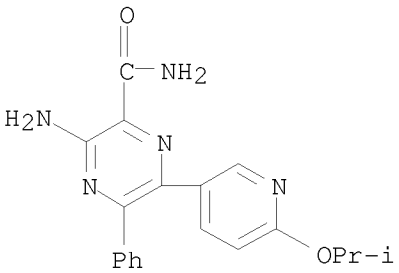
RN 851087-24-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-6-oxo-1-propyl-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



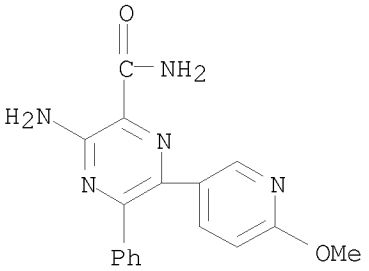
RN 851087-25-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



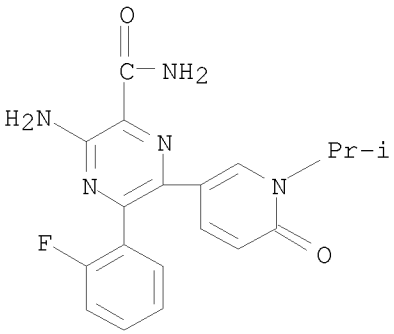
RN 851087-26-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[6-(1-methylethoxy)-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



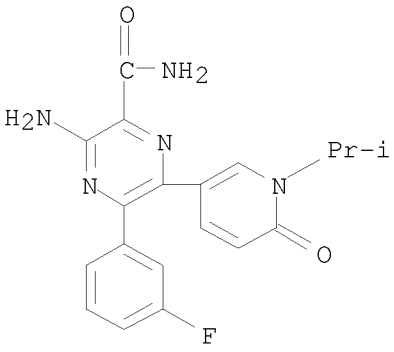
RN 851087-36-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(6-methoxy-3-pyridinyl)-5-phenyl- (9CI) (CA INDEX NAME)



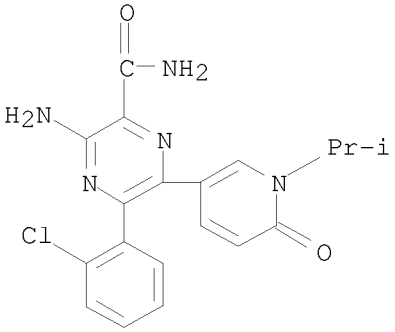
RN 851087-37-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-fluorophenyl)- (9CI) (CA INDEX NAME)



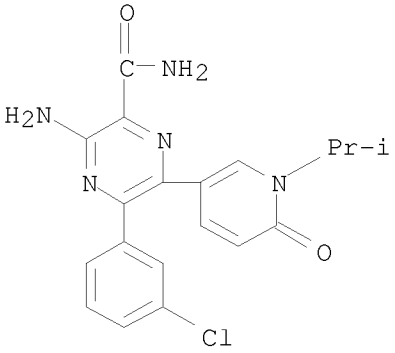
RN 851087-38-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-fluorophenyl)- (9CI) (CA INDEX NAME)



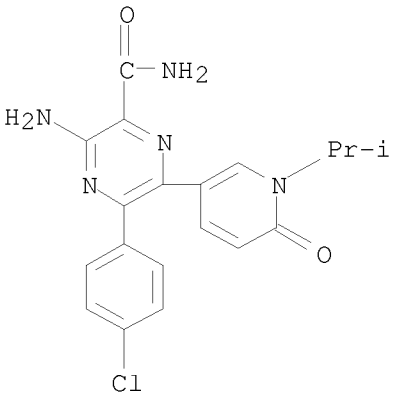
RN 851087-40-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2-chlorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



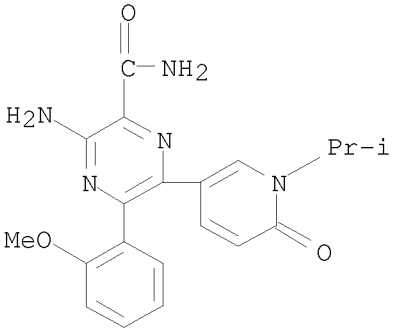
RN 851087-41-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(3-chlorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



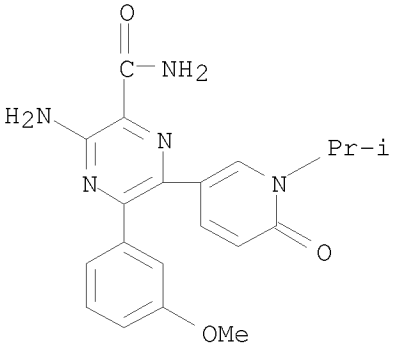
RN 851087-42-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(4-chlorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



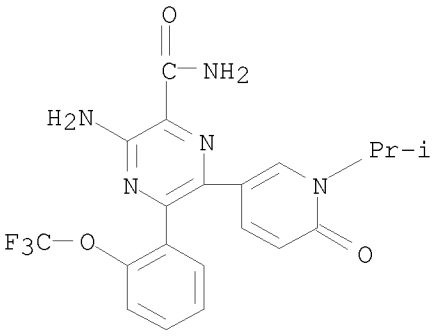
RN 851087-43-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)



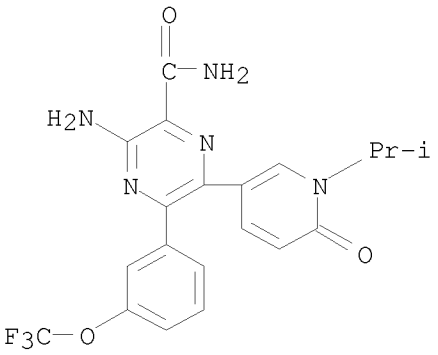
RN 851087-44-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-methoxyphenyl)- (9CI) (CA INDEX NAME)



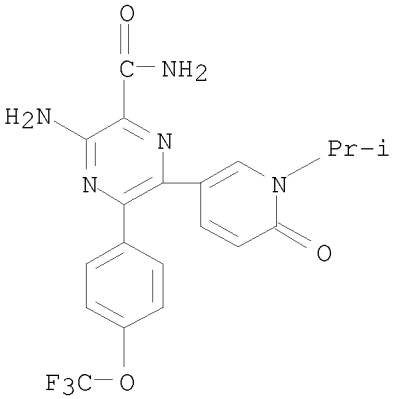
RN 851087-46-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-[2-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



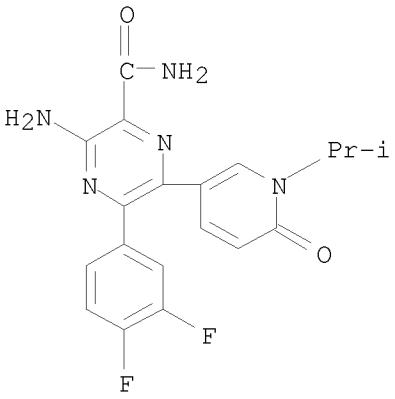
RN 851087-47-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-[3-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



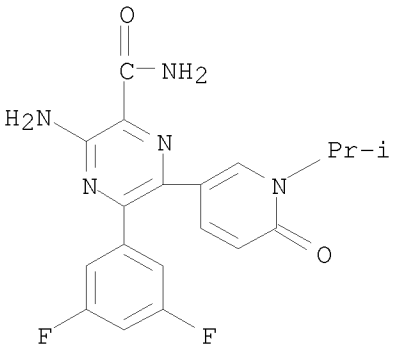
RN 851087-48-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



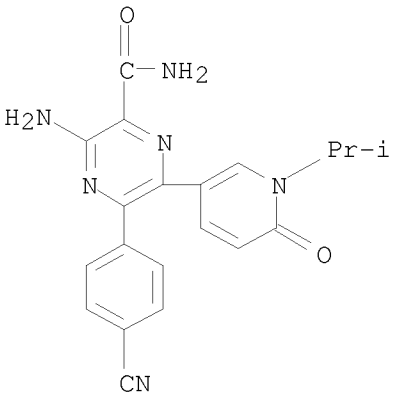
RN 851087-49-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(3,4-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



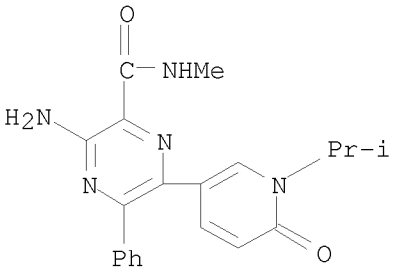
RN 851087-50-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(3,5-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



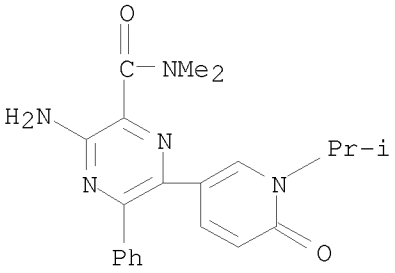
RN 851087-51-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(4-cyanophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



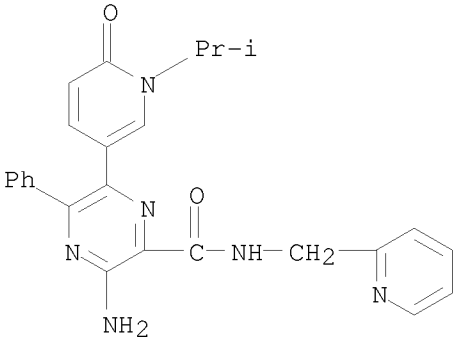
RN 851087-62-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-methyl-5-phenyl- (9CI) (CA INDEX NAME)



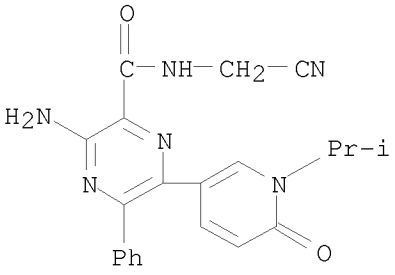
RN 851087-63-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N,N-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



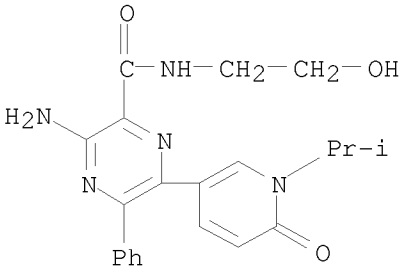
RN 851087-65-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl-N-(2-pyridinylmethyl)- (9CI) (CA INDEX NAME)



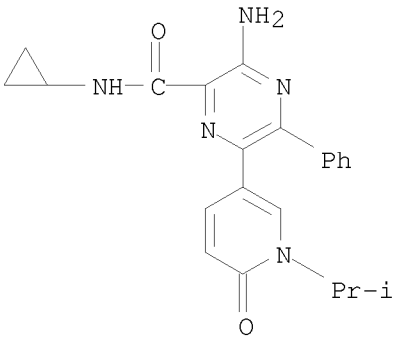
RN 851087-66-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(cyanomethyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



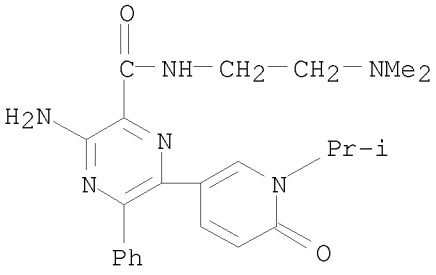
RN 851087-69-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-(2-hydroxyethyl)-5-phenyl- (9CI) (CA INDEX NAME)



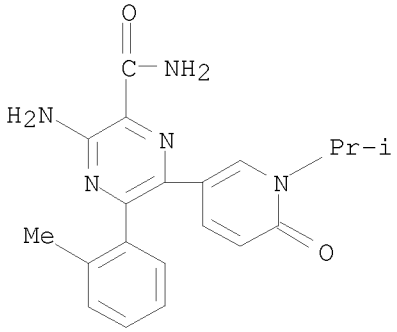
RN 851087-70-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-cyclopropyl-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-phenyl- (9CI) (CA INDEX NAME)



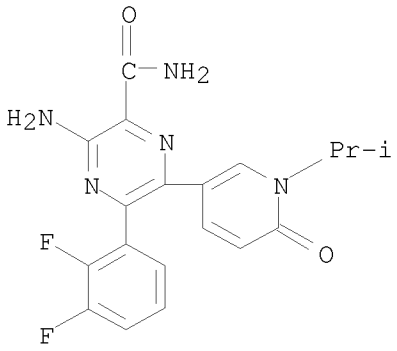
RN 851087-77-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-N-[2-(dimethylamino)ethyl]-5-phenyl- (9CI) (CA INDEX NAME)



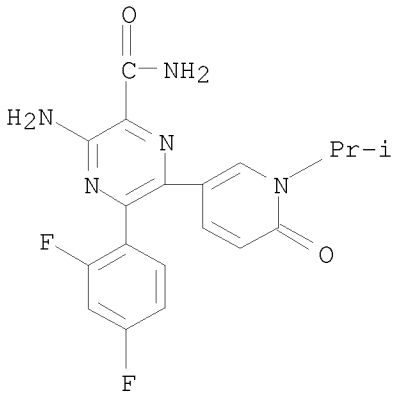
RN 851087-78-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-methylphenyl)- (9CI) (CA INDEX NAME)



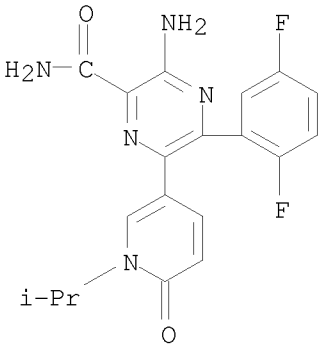
RN 851087-79-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2,3-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



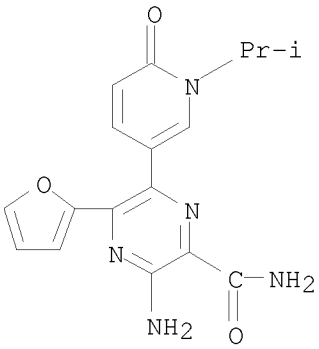
RN 851087-80-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2,4-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



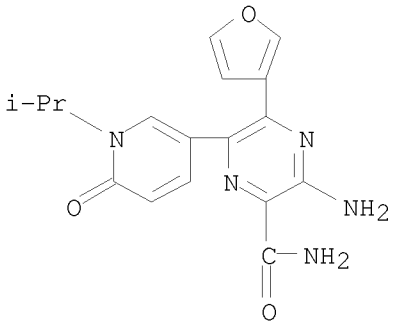
RN 851087-81-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-(2,5-difluorophenyl)-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]- (9CI) (CA INDEX NAME)



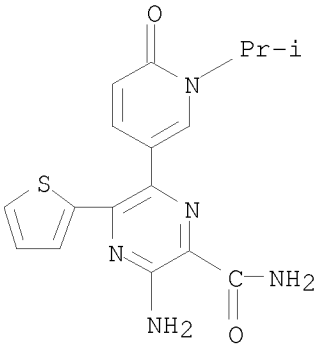
RN 851087-82-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-furanyl)- (9CI) (CA INDEX NAME)



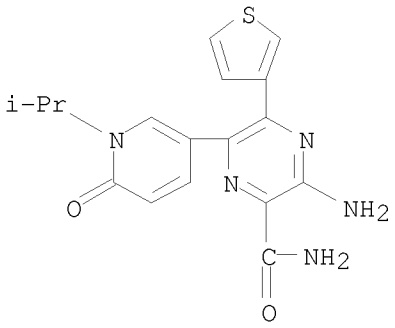
RN 851087-83-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-furanyl)- (9CI) (CA INDEX NAME)



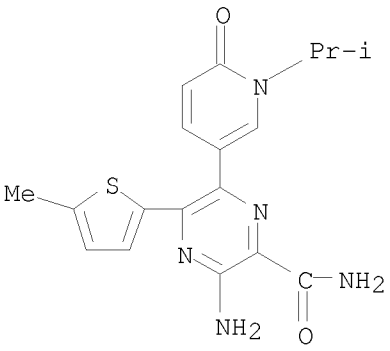
RN 851087-84-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(2-thienyl)- (9CI) (CA INDEX NAME)



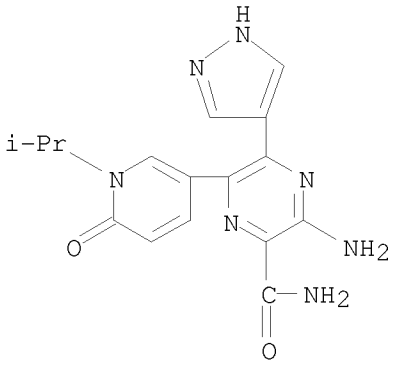
RN 851087-85-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-thienyl)- (9CI) (CA INDEX NAME)



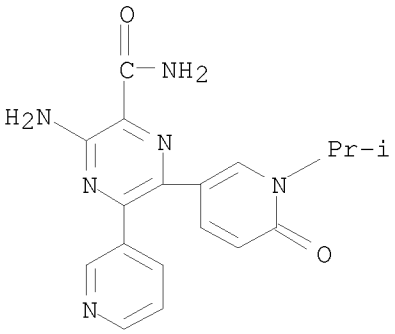
RN 851087-86-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(5-methyl-2-thienyl)- (9CI) (CA INDEX NAME)



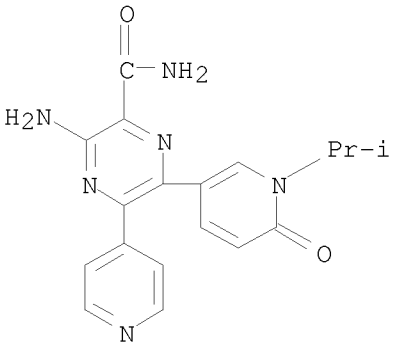
RN 851087-87-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



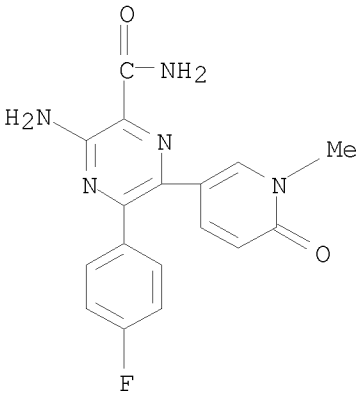
RN 851087-89-3 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(3-pyridinyl)- (9CI) (CA INDEX NAME)



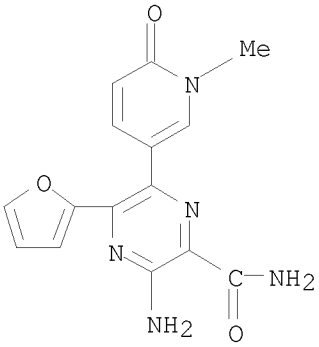
RN 851087-90-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(4-pyridinyl)- (9CI) (CA INDEX NAME)



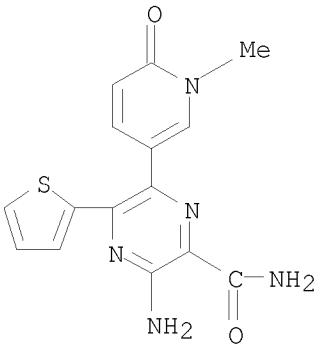
RN 851087-91-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-5-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



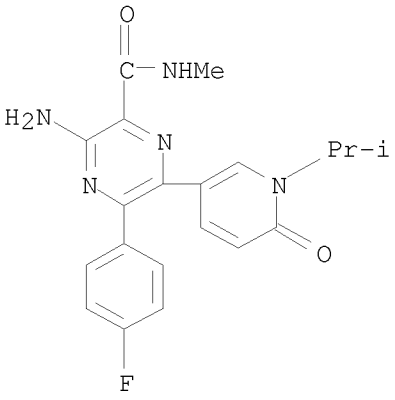
RN 851087-92-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-5-(2-furanyl)- (9CI) (CA INDEX NAME)



RN 851087-93-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-(1,6-dihydro-1-methyl-6-oxo-3-pyridinyl)-5-(2-thienyl)- (9CI) (CA INDEX NAME)



RN 851088-51-2 CAPLUS
CN Pyrazinecarboxamide, 3-amino-6-[1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl]-5-(4-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



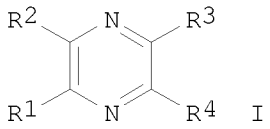

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127371 CAPLUS
DOCUMENT NUMBER: 142:56364
TITLE: Preparation of 2,3-substituted 5,6-diaryl-pyrazine derivatives as CB1 modulators
INVENTOR(S): Cheng, Leifeng; Wilstermann, Michael
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004111039 | A1 | 20041223 | WO 2004-SE968 | 20040616 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004247614 | A1 | 20041223 | AU 2004-247614 | 20040616 |
| CA 2527037 | A1 | 20041223 | CA 2004-2527037 | 20040616 |
| EP 1638956 | A1 | 20060329 | EP 2004-749010 | 20040616 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| JP 2006527769 | T | 20061207 | JP 2006-517042 | 20040616 |
| US 2007093505 | A1 | 20070426 | US 2005-561033 | 20051216 |

PRIORITY APPLN. INFO.: GB 2003-14261 A 20030619
WO 2004-SE968 W 20040616

OTHER SOURCE(S): MARPAT 142:56364
GI



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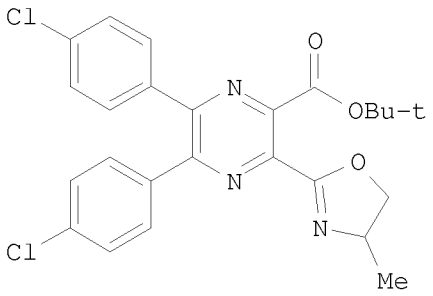


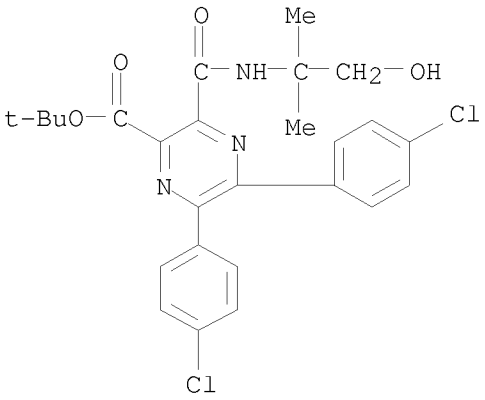
II

AB Title compds. I [wherein R1, R2 = independently (un)substituted Ph, thienyl, pyridinyl; R3, R4 = (CH2)nCO2R7, CH2OCH2R8, (CH2)qR9 with proviso, (un)substituted alkyl, etc.; R7 = (un)substituted cycloalkyl/cyclo/alkyl, (CH2)aphenyl, (un)saturated heterocyclyl; a = 0-4; R8 = (un)substituted alkyl, Ph, (un)saturated aromatic heterocyclyl; n = 0-4; q = 0-4; R9 = (un)substituted cycloalkyl, ph, aromatic heterocyclyl, saturated or partially unsatd. 5-12-membered heterocyclyl; and pharmaceutically acceptable salts thereof] were prepared as cannabinoid 1 (CB1) receptor modulators. Thus, reacting (DL)-alaninol with 5,6-Bis(4-chlorophenyl)-3-(tert-butoxycarbonyl)pyrazine-2-carboxylic acid (preparation given), followed by cyclization gave pyrazine II. I are active at the CB1 receptor (IC50 < 1 μM), most preferred compds. have IC50 < 200 nM. For instance, II exhibited an IC50 (hCB1) = 1.8 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of obesity, psychiatric and neurol. disorders (no data).

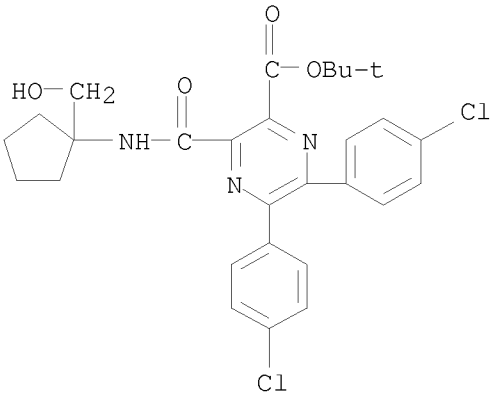
IT 811436-87-0P, 5,6-Bis(4-chlorophenyl)-3-[N-(2-hydroxy-1,1-dimethylethyl)carbamoyl]pyrazine-2-carboxylic acid tert-butyl ester 811436-90-5P, 5,6-Bis(4-chlorophenyl)-3-[N-[1-(hydroxymethyl)cyclopentyl]carbamoyl]pyrazine-2-carboxylic acid tert-butyl ester 811436-92-7P, 5,6-Bis(4-chlorophenyl)-3-[N-(2-hydroxy-1-methylethyl)carbamoyl]pyrazine-2-carboxylic acid tert-butyl ester 811436-95-0P, 5,6-Bis(4-chlorophenyl)-3-[N-(2-hydroxy-1-phenylethyl)carbamoyl]pyrazine-2-carboxylic acid tert-butyl ester 811436-98-3P, 5,6-Bis(4-chlorophenyl)-3-[N-(2-hydroxy-2-phenylethyl)carbamoyl]pyrazine-2-carboxylic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of 2,3-substituted 5,6-diaryl-pyrazines as CB1 modulators)

RN 811436-87-0 CAPLUS

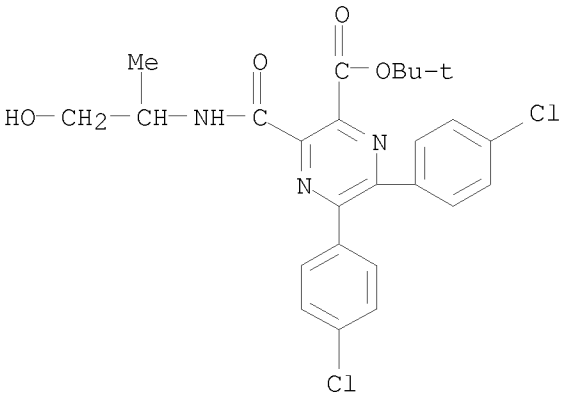
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxy-1,1-dimethylethyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 811436-90-5 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[[1-(hydroxymethyl)cyclopentyl]amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

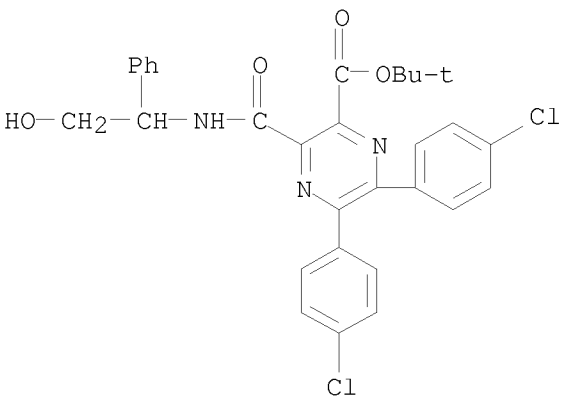


RN 811436-92-7 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxy-1-methylethyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

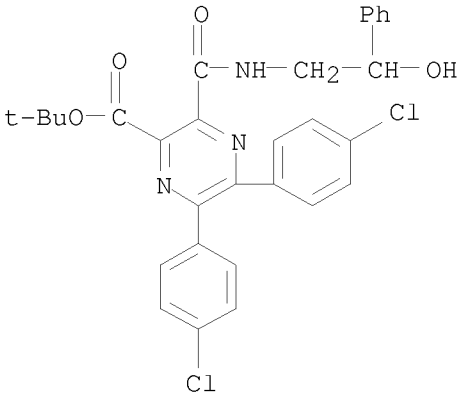


RN 811436-95-0 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxy-1-

phenylethyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 811436-98-3 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxy-2-phenylethyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

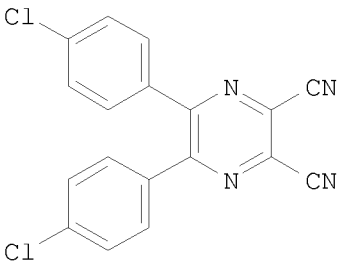


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

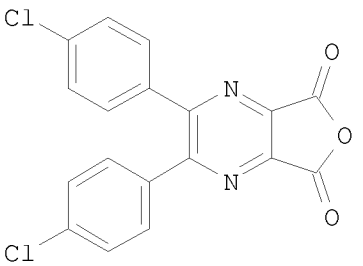
L7 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127370 CAPLUS
DOCUMENT NUMBER: 142:56363
TITLE: Preparation of 5,6-bis(4-chlorophenyl)-N-piperidin-1-yl-3-(piperidin-1-ylcarbonyl)pyrazine-2-carboxamide for treatment of obesity
INVENTOR(S): Cheng, Leifeng
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

WO 2004111038 A1 20041223 WO 2004-SE967 20040616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: GB 2003-14049 A 20030618
GI




III



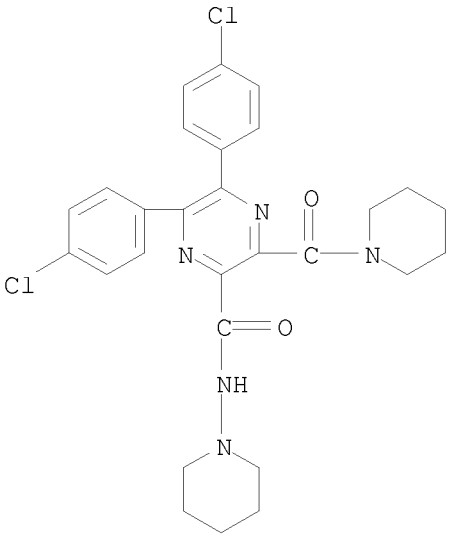

IV

AB 5,6-Bis(4-chlorophenyl)-N-piperidin-1-yl-3-(piperidin-1-yl-carbonyl)pyrazine-2-carboxamide (I) was prepared by reacting 4-ClC6H4CHO with NaCN/EtOH which gave 1,2-bis(4-chlorophenyl)-2-hydroxyethanone (II). II was oxidized to the ethane-1,2-dione which was condensed with diaminomaleonitrile to give pyrazine III. III was converted to the corresponding 2,3-dicarboxylic acid which was treated with AcCl to give furo[3,4-b]pyrazine-5,7-dione IV. IV was then subsequently reacted with piperidine/MeCN and oxalyl chloride/1-piperidinamine/CH2Cl2 to give the title compound that is intended to be used to treat obesity, psychiatric and neurol. disorders.

IT 810685-52-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bis(chlorophenyl)piperidinylpyrazinecarboxamide derivative for
treating obesity, psychiatric disorders, and neurol. disorders)

RN 810685-52-0 CAPLUS

CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-(1-piperidinylcarbonyl)- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

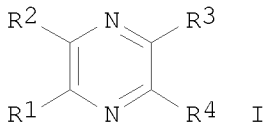
L7 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127366 CAPLUS
DOCUMENT NUMBER: 142:56362
TITLE: Preparation of 3-substituted 5,6-diaryl-pyrazine-2-carboxamide and 2-sulfonamide derivatives as cannabinoid receptor 1 (CB1) modulators
INVENTOR(S): Cheng, Leifeng
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004111034 | A1 | 20041223 | WO 2004-SE970 | 20040616 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004247616 | A1 | 20041223 | AU 2004-247616 | 20040616 |
| CA 2527035 | A1 | 20041223 | CA 2004-2527035 | 20040616 |
| EP 1638953 | A1 | 20060329 | EP 2004-749012 | 20040616 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| BR 2004011508 | A | 20060725 | BR 2004-11508 | 20040616 |
| CN 1809554 | A | 20060726 | CN 2004-80017200 | 20040616 |
| JP 2006527771 | T | 20061207 | JP 2006-517044 | 20040616 |

| | | | | | | |
|---|---|---|---|---|---|---|
| NO 2005005919 | A | 20060216 | NO 2005-5919 | | | 20051213 |
| MX 2005PA13711 | A | 20060308 | MX 2005-PA13711 | | | 20051215 |
| US 2007093484 | A1 | 20070426 | US 2005-560862 | | | 20051215 |
| PRIORITY APPLN. INFO.: | | | GB 2003-14057 | | A | 20030618 |
| | | | WO 2004-SE970 | | W | 20040616 |

OTHER SOURCE(S): MARPAT 142:56362

GI



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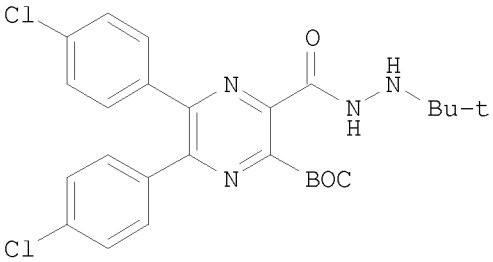


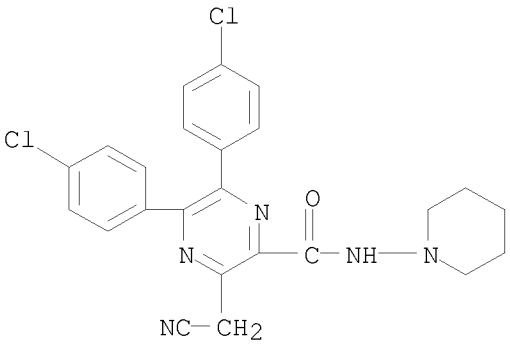
II

AB Title compds. I [wherein R1, R2 = independently (un)substituted Ph, thienyl, pyridinyl; R3 = X-Y-NR5R6; X = absent, CO, or SO2; Y = absent, NH optionally substituted by an alkyl group; R5, R6 = independently (un)substituted amino/alkyl, (CH2)r(phenyl)s, (un)saturated 5-8-membered heterocyclyl; R5 = H and R6 = defined above; or R5NR6 = (un)substituted (un)saturated 5-8-membered heterocyclyl; r = 0-4; s = 1 when r = 0, otherwise s = 1 or 2; R5NR6 = (un)substituted (un)saturated 5-8-membered heterocyclyl; R4 = (CH2)nCO2R7; n = 0-4; R7 = (un)substituted cycloalkyl/cyclo/alkyl, (CH2)nphenyl, saturated or partially unsatd. 5-8-membered heterocyclyl, CONH2 and derivs.; n = defined as above; and pharmaceutically acceptable salts thereof] were prepared as cannabinoid 1 (CB1) receptor modulators. For example, reacting 3-(tert-butoxycarbonyl)-5,6-bis(4-chlorophenyl)pyrazine-2-carboxylic acid (preparation given) with tert-butylhydrazine hydrochloride gave pyrazine II. I are active at the CB1 receptor (IC50 < 1 μM), most preferred compds. have IC50 < 200 nM. For instance, II exhibited an IC50 (hCB1) = 1.8 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of obesity, psychiatric and neurol. disorders (no data).

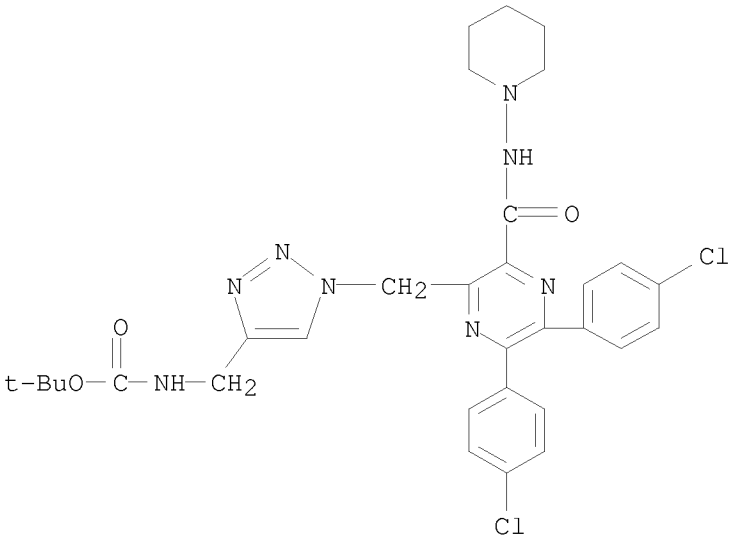
IT 811441-12-0P, 5,6-Bis(4-chlorophenyl)-3-(cyanomethyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-34-6P, tert-Butyl [[1-[[5,6-bis(4-chlorophenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazin-2-yl]methyl]-1H-1,2,3-triazol-4-yl]methyl]carbamate 811441-35-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of 3-substituted 5,6-diarylpyrazine-2-carboxamide and 2-sulfonamide derivs. as CB1 modulators)

RN 811441-12-0 CAPLUS

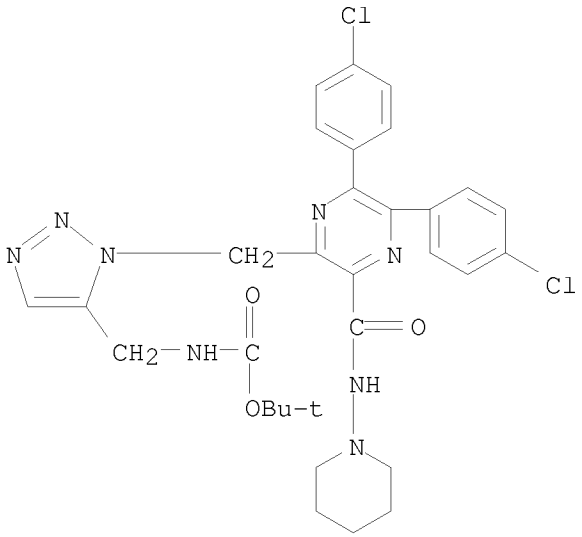
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-(cyanomethyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)



RN 811441-34-6 CAPLUS
CN Carbamic acid, [[1-[[5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]pyrazinyl]methyl]-1H-1,2,3-triazol-4-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 811441-35-7 CAPLUS
CN Carbamic acid, [[1-[[5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]pyrazinyl]methyl]-1H-1,2,3-triazol-5-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

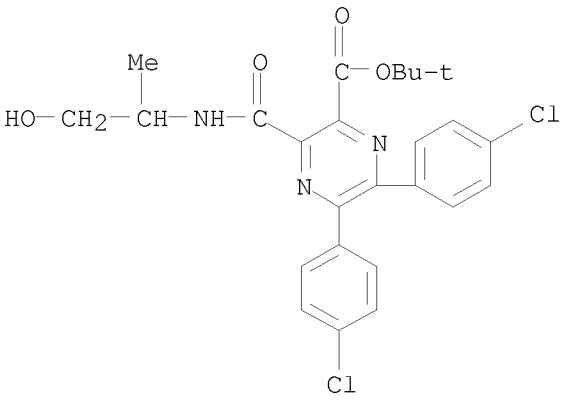



IT 811436-92-7P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxy-1-methylethyl)amino]carbonyl]pyrazine-2-carboxylate 811440-95-6P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811440-96-7P, Butyl 5,6-bis(4-chlorophenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811440-97-8P, Cyclohexyl 5,6-bis(4-chlorophenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811440-98-9P, Benzyl 5,6-bis(4-chlorophenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811440-99-0P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(cis-2-hydroxycyclohexyl)amino]carbonyl]pyrazine-2-carboxylate 811441-00-6P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(trans-2-hydroxycyclohexyl)amino]carbonyl]pyrazine-2-carboxylate 811441-01-7P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[2-[4-(trifluoromethyl)phenyl]hydrazino]carbonyl]pyrazine-2-carboxylate 811441-02-8P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(morpholin-4-yl)amino]carbonyl]pyrazine-2-carboxylate 811441-03-9P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[2-(tert-butyl)hydrazino]carbonyl]pyrazine-2-carboxylate 811441-04-0P, 3-(tert-Butoxymethyl)-5,6-bis(4-chlorophenyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-08-4P, 5,6-Bis(4-chlorophenyl)-3-[(cyclohexylidene)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-17-5P, 5,6-Bis(4-chlorophenyl)-3-(1-methoxyethyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-22-2P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(4,4-difluorocyclohexyl)amino]carbonyl]pyrazine-2-carboxylate 811441-23-3P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[(pentylamino)carbonyl]pyrazine-2-carboxylate 811441-24-4P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(1-ethylpropyl)amino]carbonyl]pyrazine-2-carboxylate 811441-25-5P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(4,4-difluoropiperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811441-27-7P, 5,6-Bis(4-chlorophenyl)-N-(piperidin-1-yl)-3-[(4-propyl-1H-1,2,3-triazol-1-yl)methyl]pyrazine-2-carboxamide 811441-32-4P, 5,6-Bis(4-chlorophenyl)-3-[[5-(1-hydroxyethyl)-1H-1,2,3-triazol-1-yl]methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-36-8P, 3-[[4-(Aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide hydrochloride 811441-37-9P, 3-[[5-(Aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide hydrochloride 811441-38-0P, 5,6-Bis(4-chlorophenyl)-3-(phenoxymethyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide

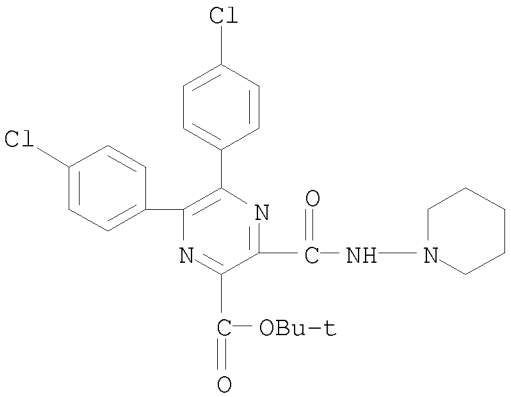
811441-40-4P, 5,6-Bis(4-chlorophenyl)-3-[(morpholin-4-yl)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-42-6P, 5,6-Bis(4-chlorophenyl)-3-[(piperidin-1-yl)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-44-8P, 5,6-Bis(4-chlorophenyl)-3-[[(cyclohex-2-en-1-yl)oxy]methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-47-1P, 5,6-Bis(4-chlorophenyl)-3-[(cyclohexyloxy)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-50-6P, 5,6-Bis(4-chlorophenyl)-N-(2-hydroxyethyl)-N'-(piperidin-1-yl)pyrazine-2,3-dicarboxamide 811441-52-8P, 5,6-Bis(4-chlorophenyl)-N-(3-hydroxybutyl)-N'-(piperidin-1-yl)pyrazine-2,3-dicarboxamide 811441-53-9P, 5,6-Bis(4-chlorophenyl)-N-(3-hydroxypropyl)-N'-(piperidin-1-yl)pyrazine-2,3-dicarboxamide 811441-54-0P, tert-Butyl 5,6-bis(4-methylphenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811441-58-4P, 5,6-Bis(4-methylphenyl)-N-(piperidin-1-yl)-3-[(1H-tetrazol-1-yl)methyl]pyrazine-2-carboxamide 811441-62-0P, 5,6-Bis(4-methylphenyl)-N-(piperidin-1-yl)-3-[(2H-tetrazol-2-yl)methyl]pyrazine-2-carboxamide 811441-64-2P, 5,6-Bis(4-chlorophenyl)-N-(piperidin-1-yl)-3-[(2H-tetrazol-2-yl)methyl]pyrazine-2-carboxamide 811441-65-3P, 5,6-Bis(4-chlorophenyl)-N-(piperidin-1-yl)-3-[(1H-tetrazol-1-yl)methyl]pyrazine-2-carboxamide 811441-66-4P, 5,6-Bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-[(2H-tetrazol-2-yl)methyl]pyrazine-2-carboxamide 811441-67-5P, 5,6-Bis(4-chlorophenyl)-N-(4,4-difluoropiperidin-1-yl)-3-[(2H-tetrazol-2-yl)methyl]pyrazine-2-carboxamide 811441-68-6P, 5,6-Bis(4-chlorophenyl)-3-[(2-methoxyethoxy)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-71-1P, 5,6-Bis(4-chlorophenyl)-3-[(5-cyclopropyl-2H-tetrazol-2-yl)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-74-4P, 5,6-Bis(4-chlorophenyl)-3-[(5-cyclopropyl-1H-tetrazol-1-yl)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-75-5P, 5,6-Bis(4-chlorophenyl)-3-[(5-methyl-2H-tetrazol-2-yl)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-78-8P, 5,6-Bis(4-chlorophenyl)-3-[(5-methyl-1H-tetrazol-1-yl)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811441-79-9P , tert-Butyl 6-(4-chlorophenyl)-5-(4-methylphenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811441-86-8P, tert-Butyl 5-(4-chlorophenyl)-6-(4-methylphenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylate 811441-87-9P, 6-(4-Chlorophenyl)-5-(4-methylphenyl)-N-(piperidin-1-yl)-3-[(2H-tetrazol-2-yl)methyl]pyrazine-2-carboxamide 811441-94-8P, 5-(4-Chlorophenyl)-6-(4-methylphenyl)-N-(piperidin-1-yl)-3-[(2H-tetrazol-2-yl)methyl]pyrazine-2-carboxamide 811441-97-1P, tert-Butyl 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxyethyl)(methyl)amino]carbonyl]pyrazine-2-carboxylate 811441-98-2P, 5,6-Bis(4-chlorophenyl)-3-propoxypyrazine-2-carboxylic acid N-(piperidin-1-yl)amide 811442-03-2P, 5,6-Bis(4-chlorophenyl)-N-(piperidin-1-yl)-3-[(2H-tetrazol-5-yl)methyl]pyrazine-2-carboxamide 811442-07-6P, 5,6-Bis(4-chlorophenyl)-3-[[5-(morpholin-4-yl)-2H-tetrazol-2-yl]methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-08-7P, 5,6-Bis(4-chlorophenyl)-3-[[5-(morpholin-4-yl)-1H-tetrazol-1-yl]methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-10-1P, 5,6-Bis(4-chlorophenyl)-N-(piperidin-1-yl)-3-[[5-(pyrrolidin-1-yl)-2H-tetrazol-2-yl]methyl]pyrazine-2-carboxamide 811442-11-2P, 5,6-Bis(4-chlorophenyl)-N-(piperidin-1-yl)-3-[[5-(pyrrolidin-1-yl)-1H-tetrazol-1-yl]methyl]pyrazine-2-carboxamide 811442-12-3P, 5,6-Bis(4-chlorophenyl)-3-[[5-(methylthio)-2H-tetrazol-2-yl]methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-13-4P, 5,6-Bis(4-chlorophenyl)-3-[[5-(methylthio)-1H-tetrazol-1-yl]methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-14-5P, 5,6-Bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-(methoxymethyl)pyrazine-2-carboxamide 811442-16-7P,

5,6-Bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-[[(4-fluorobenzyl)oxy]methyl]pyrazine-2-carboxamide 811442-19-0P, 5,6-Bis(4-chlorophenyl)-3-[(4,4-difluoropiperidin-1-yl)methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-21-4P, 5,6-Bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-[(4,4-difluoropiperidin-1-yl)methyl]pyrazine-2-carboxamide 811442-22-5P, 5,6-Bis(4-chlorophenyl)-N-(4,4-difluoropiperidin-1-yl)-3-(methoxymethyl)pyrazine-2-carboxamide 811442-24-7P, 5,6-Bis(4-chlorophenyl)-3-[[4-(1-hydroxyethyl)-1H-1,2,3-triazol-1-yl]methyl]-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-25-8P, 3-[[4-(Aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-26-9P, 3-[[5-(Aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 3-substituted 5,6-diarylpyrazine-2-carboxamide and 2-sulfonamide derivs. as CB1 modulators)

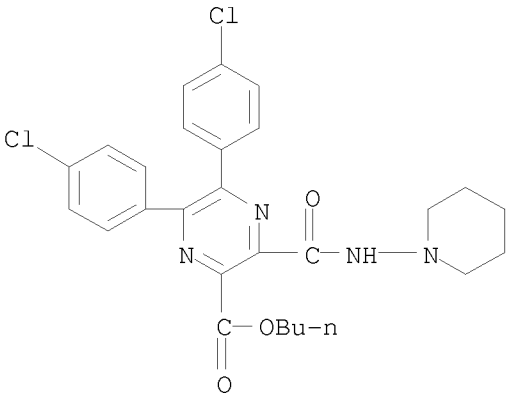
RN 811436-92-7 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxy-1-methylethyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



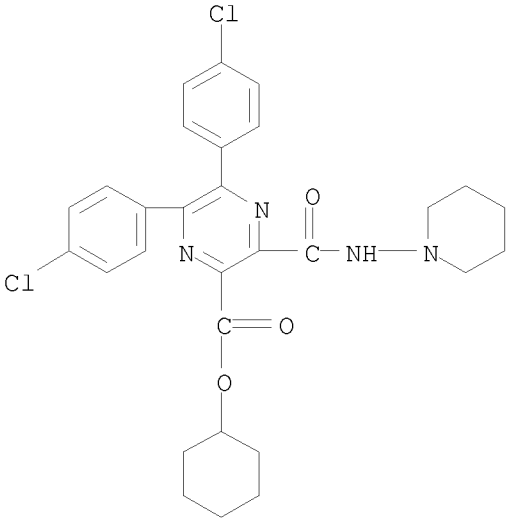

RN 811440-95-6 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



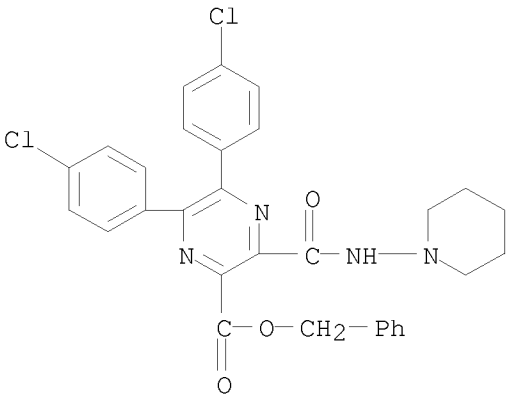
RN 811440-96-7 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]-, butyl ester (9CI) (CA INDEX NAME)




RN 811440-97-8 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]-, cyclohexyl ester (9CI) (CA INDEX NAME)

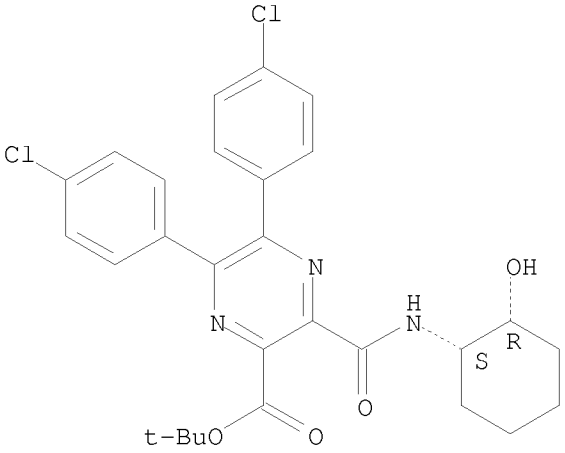



RN 811440-98-9 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



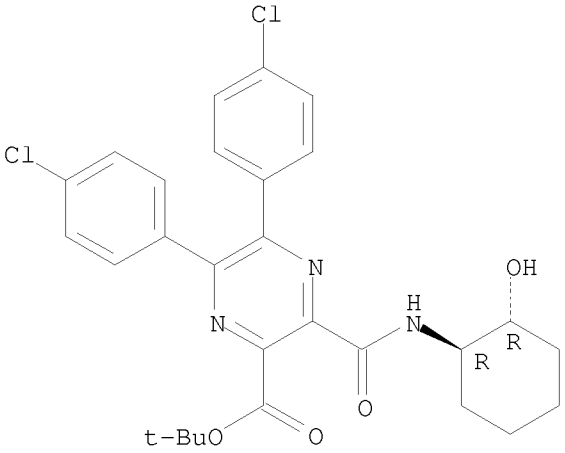

RN 811440-99-0 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[[(1R,2S)-2-hydroxycyclohexyl]amino]carbonyl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

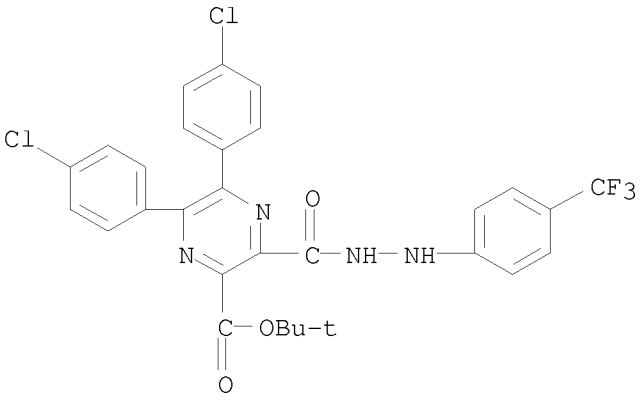



RN 811441-00-6 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[[(1R,2R)-2-hydroxycyclohexyl]amino]carbonyl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

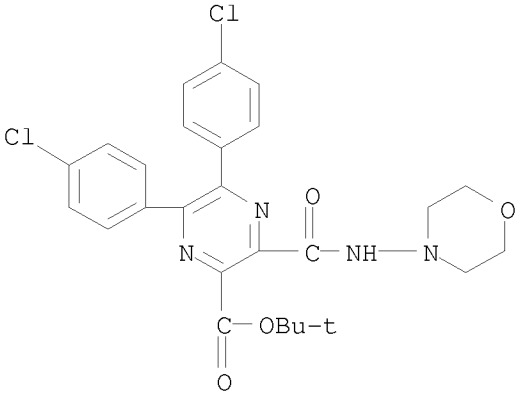
Relative stereochemistry.



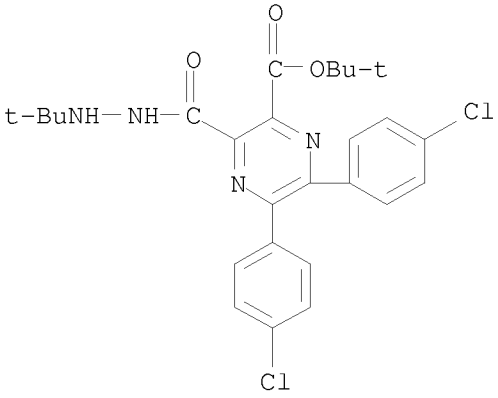

RN 811441-01-7 CAPLUS
CN 2,3-Pyrazinedicarboxylic acid, 5,6-bis(4-chlorophenyl)-, mono(1,1-dimethylethyl) ester, 2-[4-(trifluoromethyl)phenyl]hydrazide (9CI) (CA INDEX NAME)



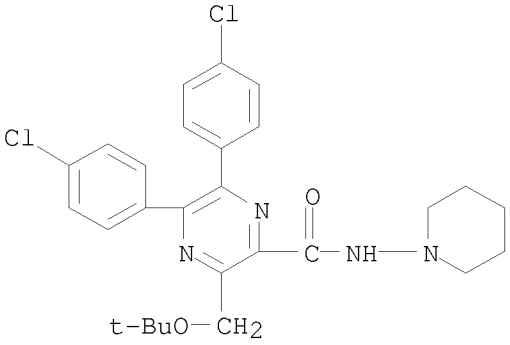

RN 811441-02-8 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(4-morpholinylamino)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



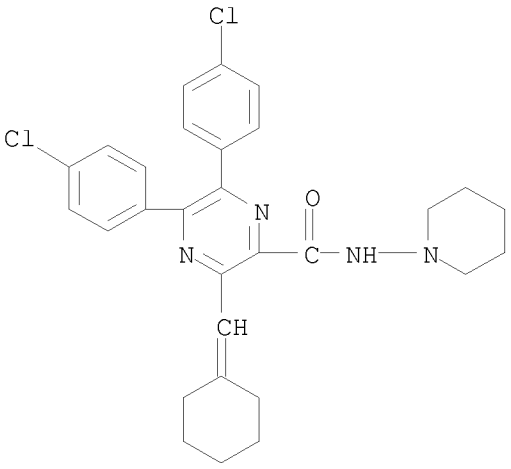
RN 811441-03-9 CAPLUS
CN 2,3-Pyrazinedicarboxylic acid, 5,6-bis(4-chlorophenyl)-, mono(1,1-dimethylethyl) ester, 2-(1,1-dimethylethyl)hydrazide (9CI) (CA INDEX NAME)



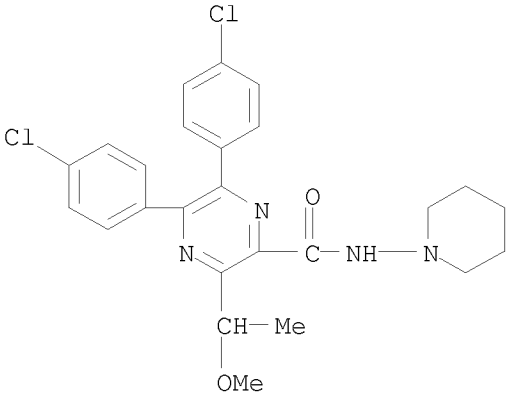

RN 811441-04-0 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(1,1-dimethylethoxy)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



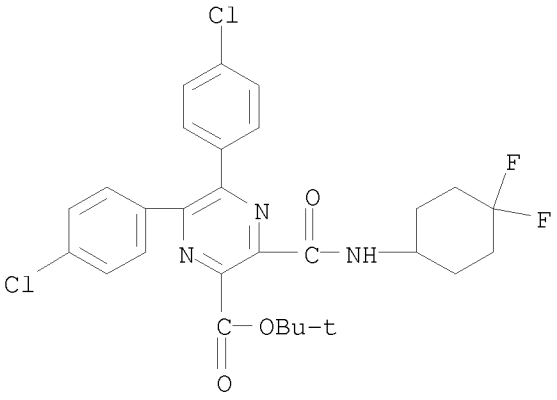

RN 811441-08-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-(cyclohexylidenemethyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)



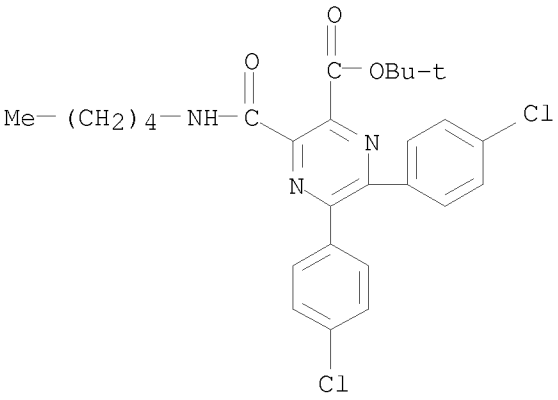
RN 811441-17-5 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-(1-methoxyethyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)



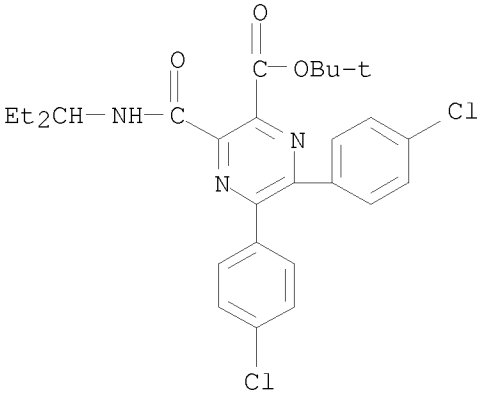
RN 811441-22-2 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(4,4-difluorocyclohexyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



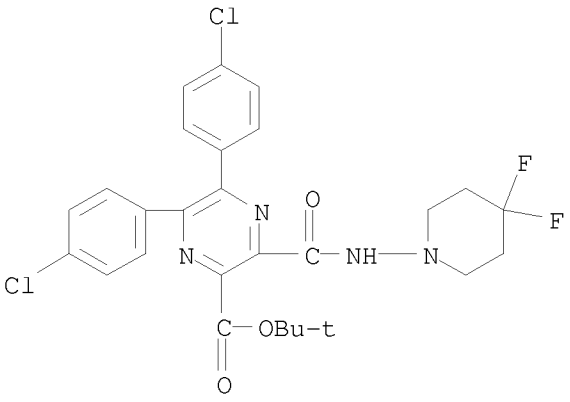
RN 811441-23-3 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(pentylamino)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



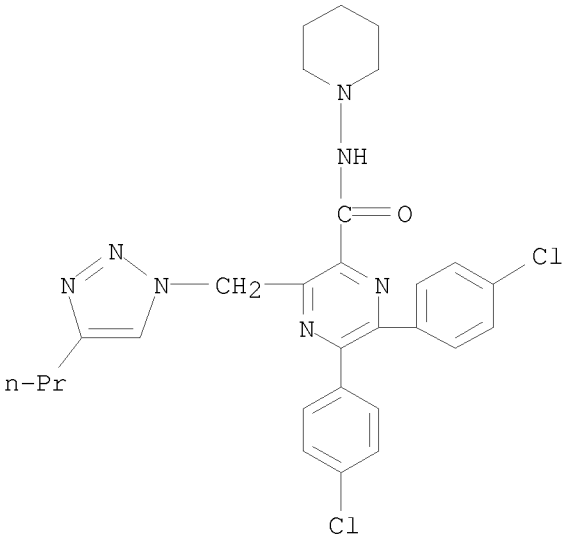
RN 811441-24-4 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(1-ethylpropyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



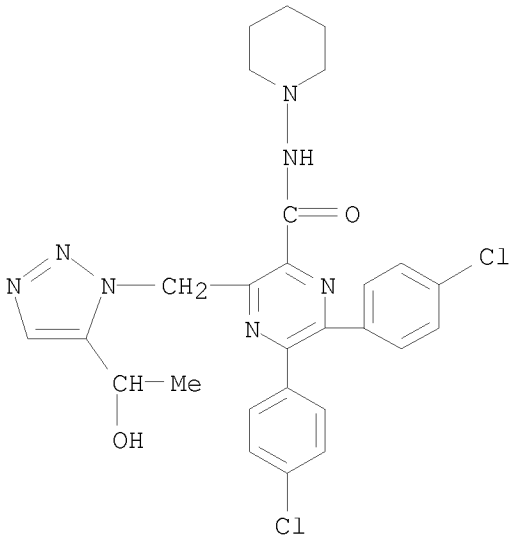
RN 811441-25-5 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(4,4-difluoro-1-piperidinyl)amino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



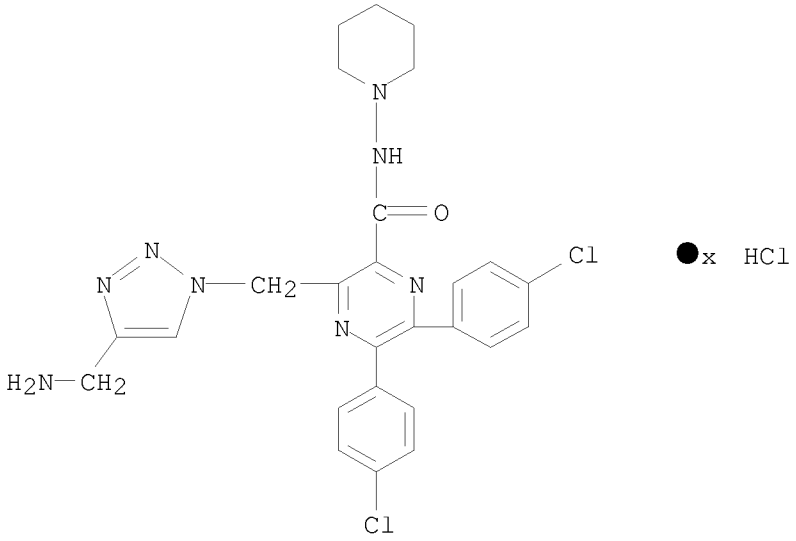

RN 811441-27-7 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-[(4-propyl-1H-1,2,3-triazol-1-yl)methyl]- (9CI) (CA INDEX NAME)



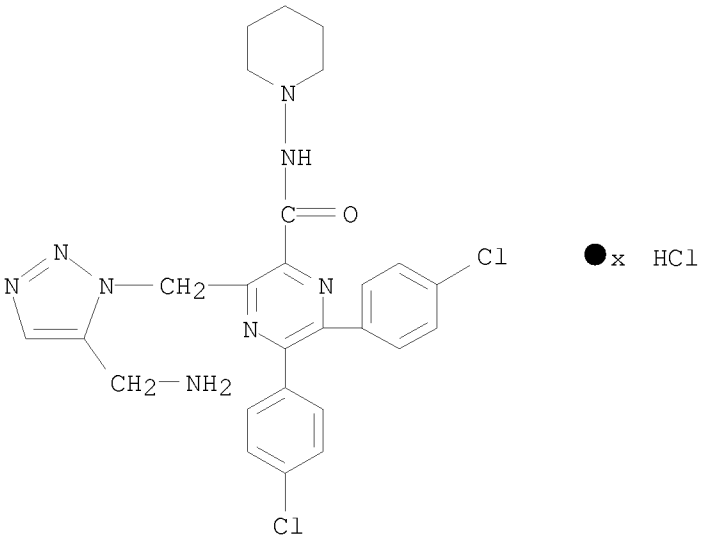

RN 811441-32-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[[5-(1-hydroxyethyl)-1H-1,2,3-triazol-1-yl]methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



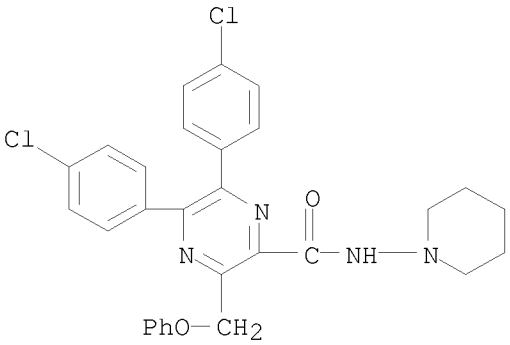
RN 811441-36-8 CAPLUS
CN Pyrazinecarboxamide, 3-[[4-(aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-1-piperidinyl-, hydrochloride (9CI) (CA INDEX NAME)



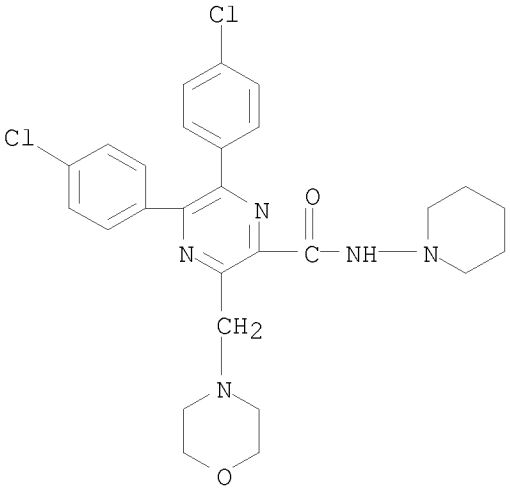
RN 811441-37-9 CAPLUS
CN Pyrazinecarboxamide, 3-[[5-(aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-1-piperidinyl-, hydrochloride (9CI) (CA INDEX NAME)



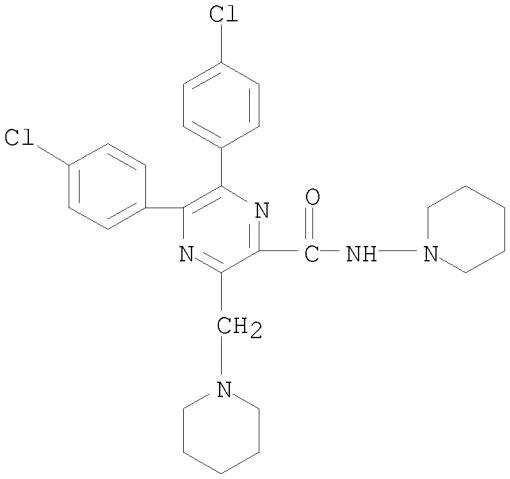
RN 811441-38-0 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-(phenoxymethyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)



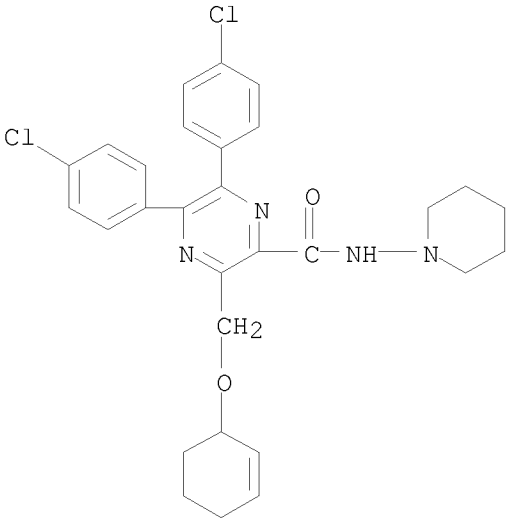
RN 811441-40-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-(4-morpholinylmethyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)



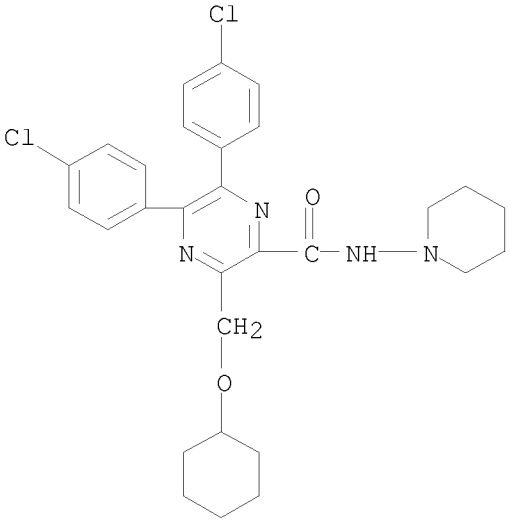

RN 811441-42-6 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



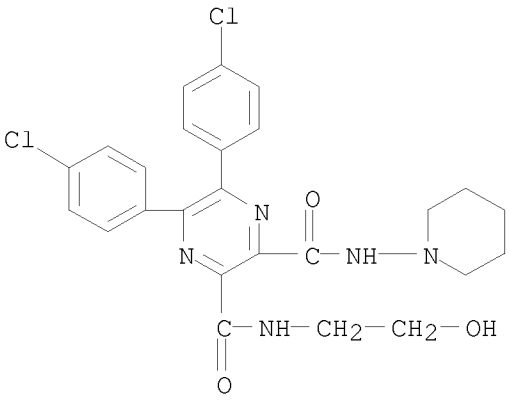

RN 811441-44-8 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(2-cyclohexen-1-yloxy)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



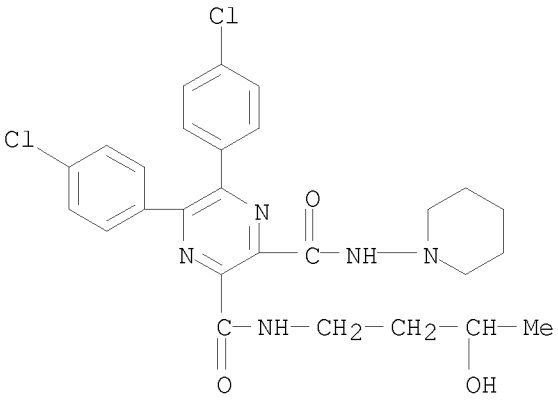
RN 811441-47-1 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(cyclohexyloxy)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



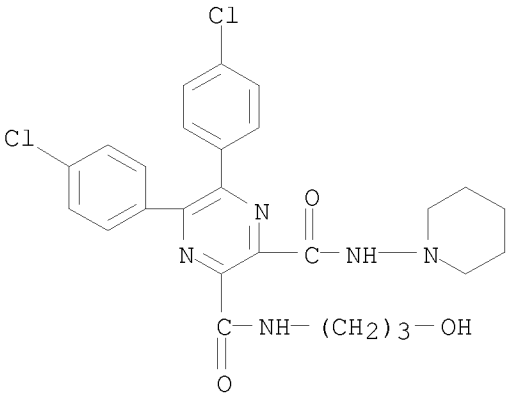
RN 811441-50-6 CAPLUS
CN 2,3-Pyrazinedicarboxamide, 5,6-bis(4-chlorophenyl)-N-(2-hydroxyethyl)-N'-1-piperidinyl- (9CI) (CA INDEX NAME)



RN 811441-52-8 CAPLUS
CN 2,3-Pyrazinedicarboxamide, 5,6-bis(4-chlorophenyl)-N-(3-hydroxybutyl)-N'-1-piperidinyl- (9CI) (CA INDEX NAME)

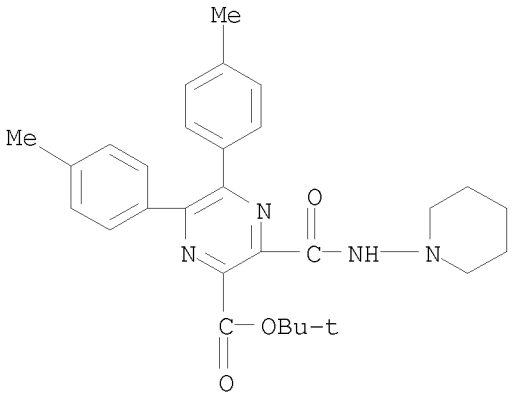


RN 811441-53-9 CAPLUS
CN 2,3-Pyrazinedicarboxamide, 5,6-bis(4-chlorophenyl)-N-(3-hydroxypropyl)-N'-1-piperidinyl- (9CI) (CA INDEX NAME)

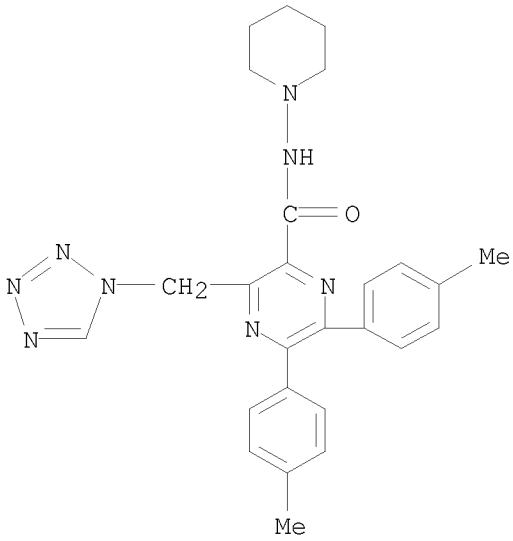


RN 811441-54-0 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-methylphenyl)-3-[(1-piperidinylamino)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX

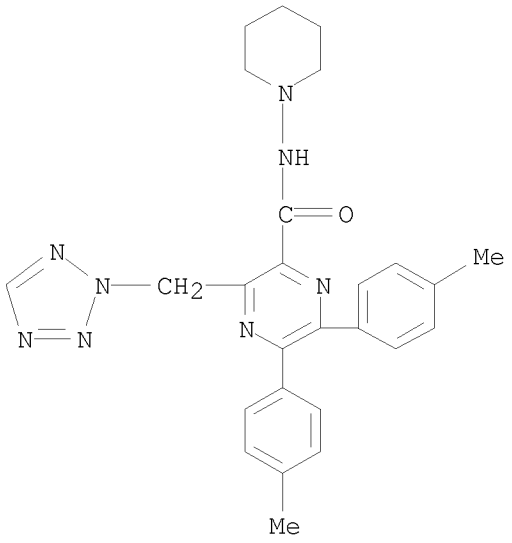
NAME)



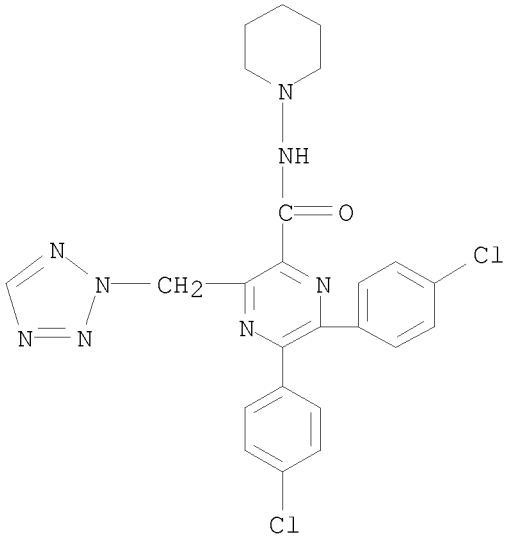

RN 811441-58-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-methylphenyl)-N-1-piperidinyl-3-(1H-tetrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



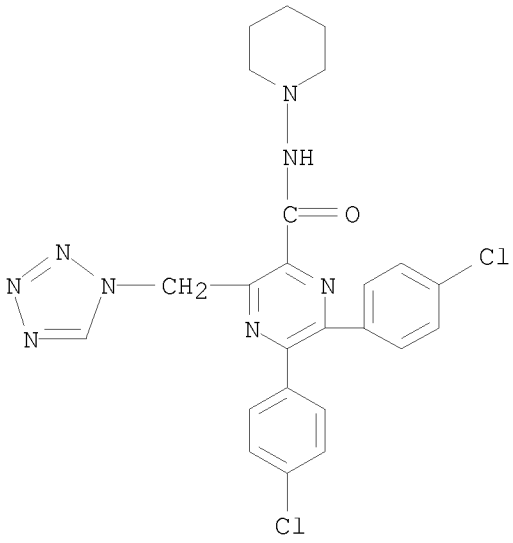

RN 811441-62-0 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-methylphenyl)-N-1-piperidinyl-3-(2H-tetrazol-2-ylmethyl)- (9CI) (CA INDEX NAME)



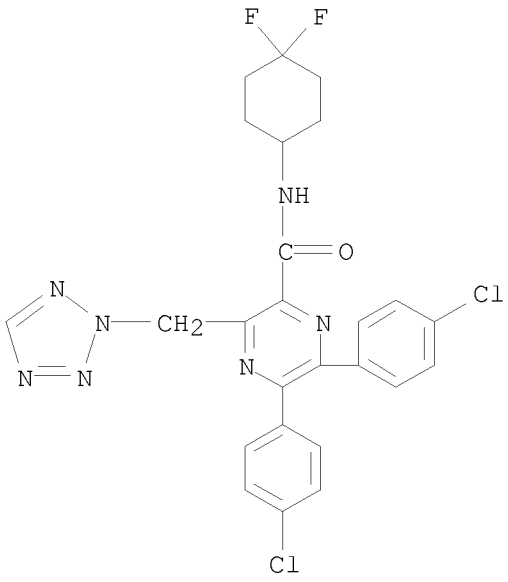
RN 811441-64-2 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-(2H-tetrazol-2-ylmethyl)- (9CI) (CA INDEX NAME)



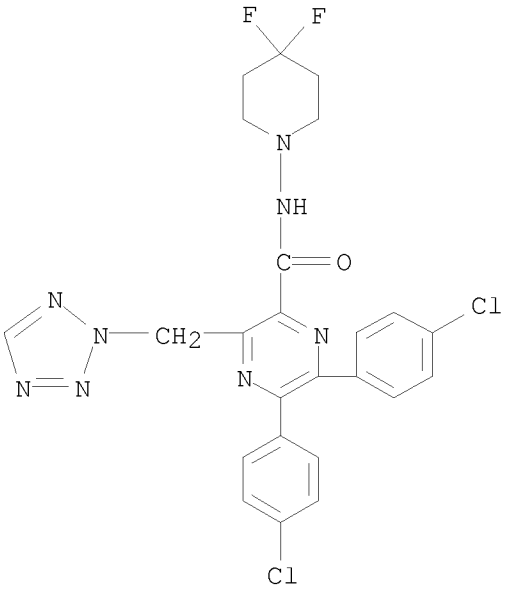
RN 811441-65-3 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-(1H-tetrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



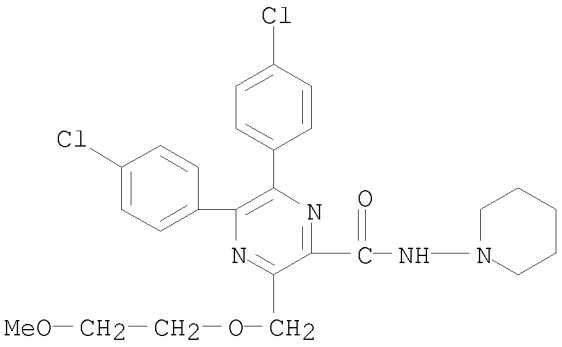
RN 811441-66-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-(2H-tetrazol-2-ylmethyl)- (9CI) (CA INDEX NAME)



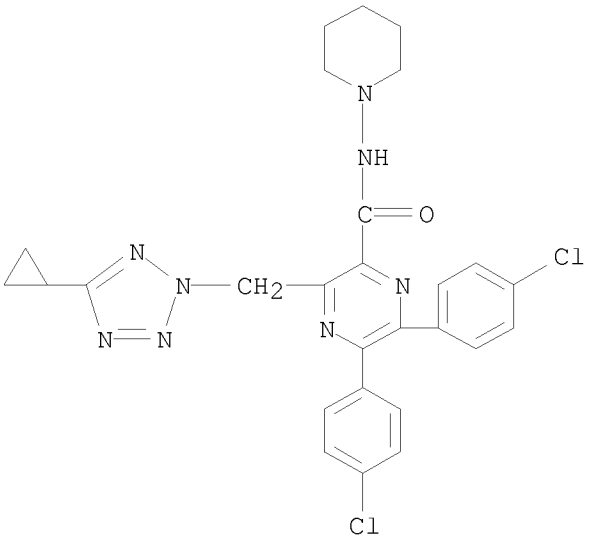
RN 811441-67-5 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-(4,4-difluoro-1-piperidinyl)-3-(2H-tetrazol-2-ylmethyl)- (9CI) (CA INDEX NAME)



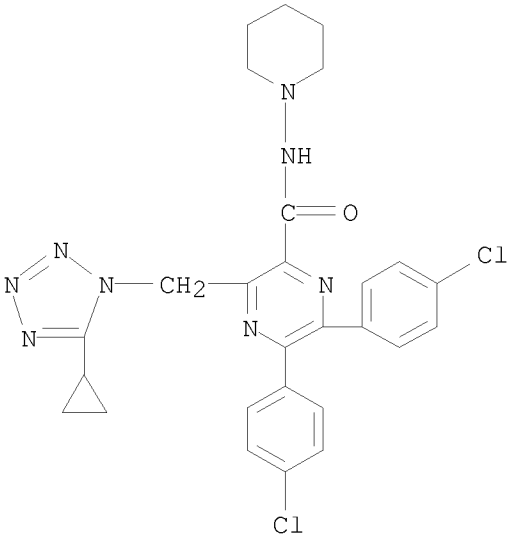
RN 811441-68-6 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(2-methoxyethoxy)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



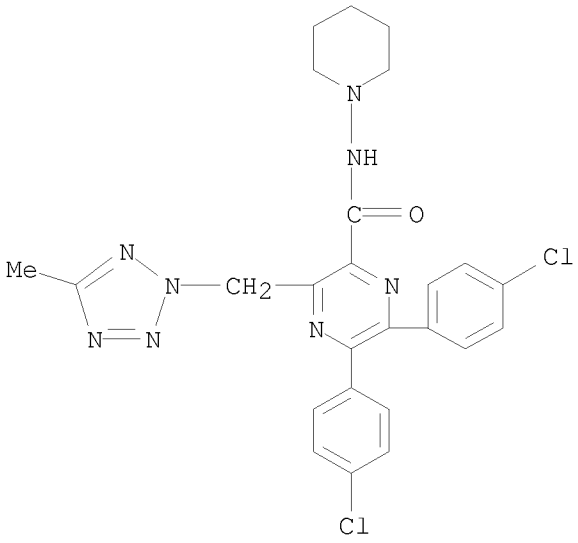
RN 811441-71-1 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(5-cyclopropyl-2H-tetrazol-2-yl)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



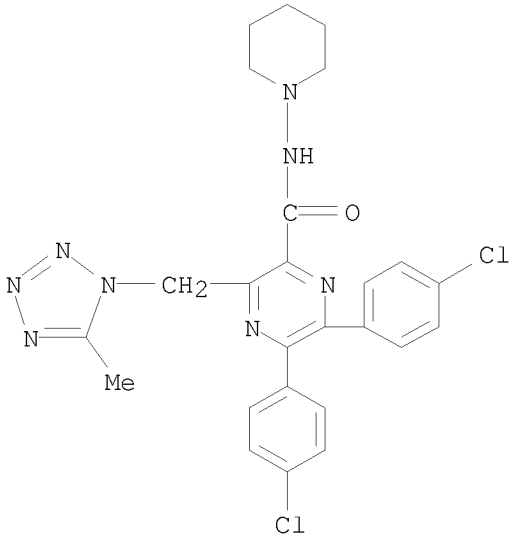
RN 811441-74-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(5-cyclopropyl-1H-tetrazol-1-yl)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



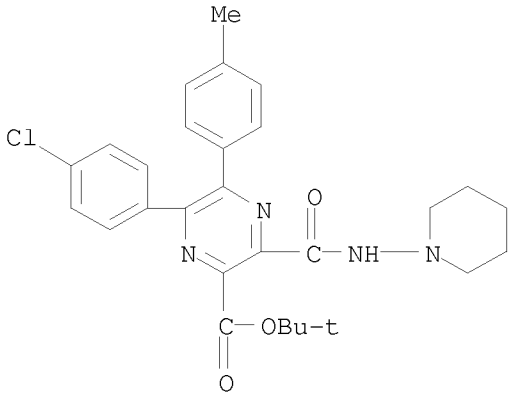
RN 811441-75-5 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(5-methyl-2H-tetrazol-2-yl)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



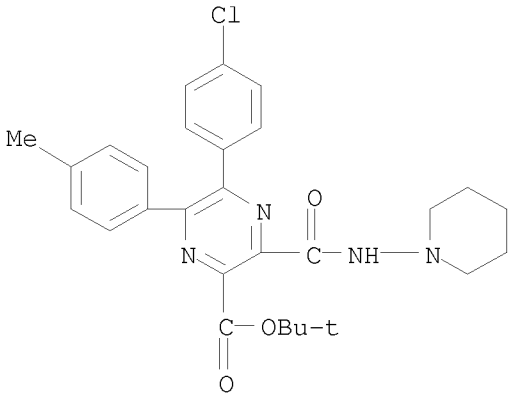
RN 811441-78-8 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(5-methyl-1H-tetrazol-1-yl)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



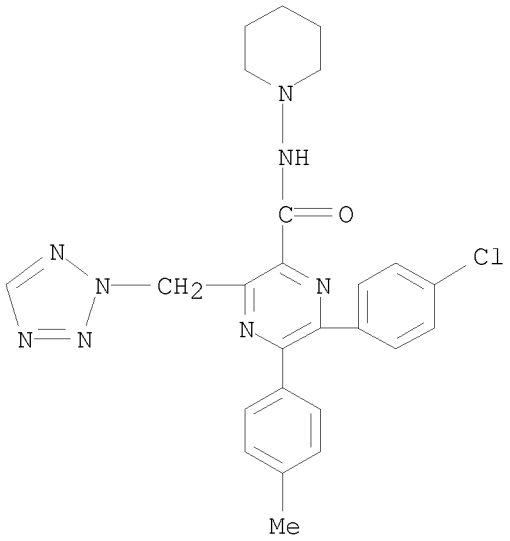
RN 811441-79-9 CAPLUS
CN Pyrazinecarboxylic acid, 6-(4-chlorophenyl)-5-(4-methylphenyl)-3-[(1-piperidinylamino)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



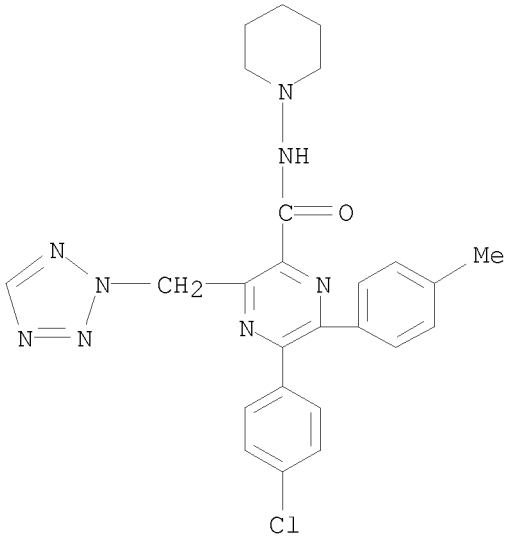

RN 811441-86-8 CAPLUS
CN Pyrazinecarboxylic acid, 5-(4-chlorophenyl)-6-(4-methylphenyl)-3-[(1-piperidinylamino)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



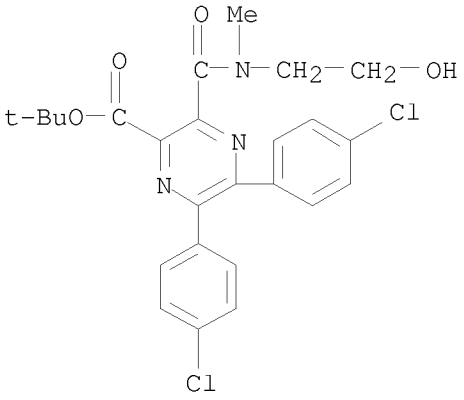

RN 811441-87-9 CAPLUS
CN Pyrazinecarboxamide, 6-(4-chlorophenyl)-5-(4-methylphenyl)-N-1-piperidinyl-3-(2H-tetrazol-2-ylmethyl)- (9CI) (CA INDEX NAME)



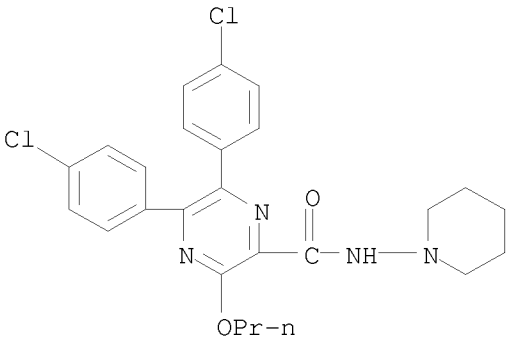

RN 811441-94-8 CAPLUS
CN Pyrazinecarboxamide, 5-(4-chlorophenyl)-6-(4-methylphenyl)-N-1-piperidinyl-3-(2H-tetrazol-2-ylmethyl)- (9CI) (CA INDEX NAME)



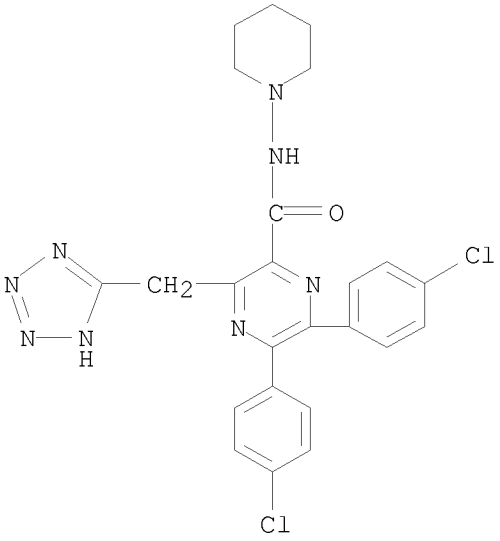

RN 811441-97-1 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[[(2-hydroxyethyl)methylamino]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



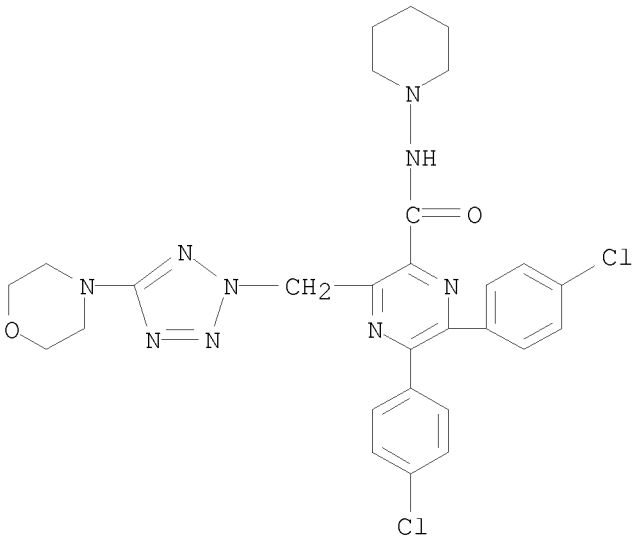
RN 811441-98-2 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-propoxy- (9CI) (CA INDEX NAME)



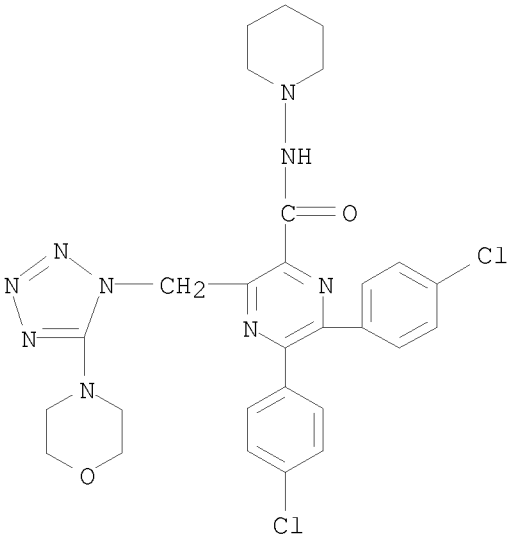
RN 811442-03-2 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-(1H-tetrazol-5-ylmethyl)- (9CI) (CA INDEX NAME)



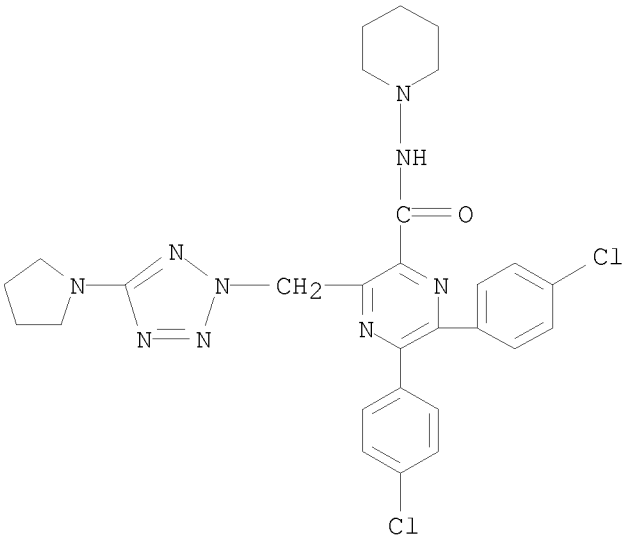
RN 811442-07-6 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[[5-(4-morpholinyl)-2H-tetrazol-2-yl]methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



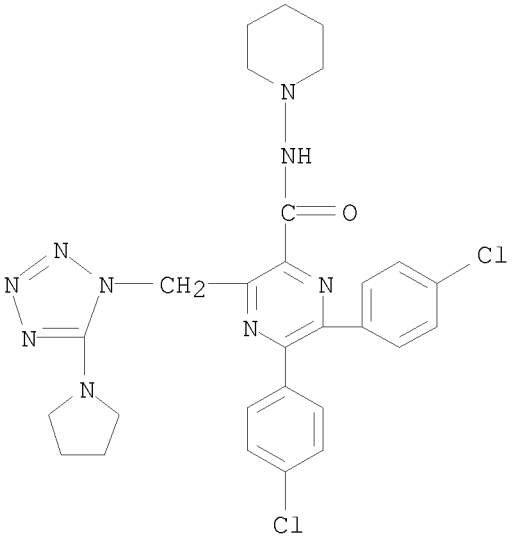
RN 811442-08-7 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[[5-(4-morpholinyl)-1H-tetrazol-1-yl]methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



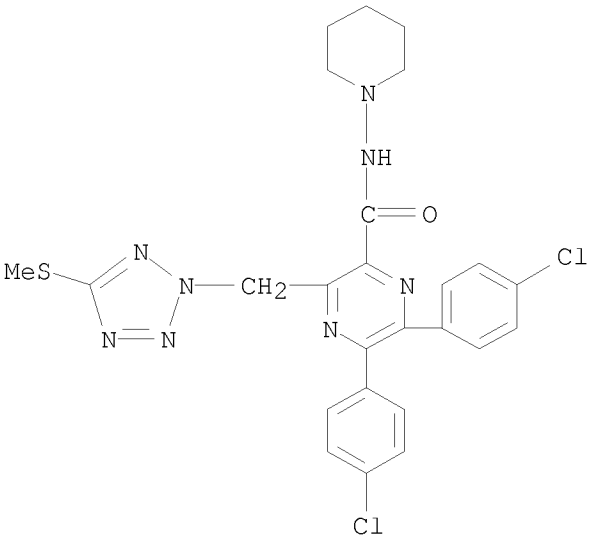
RN 811442-10-1 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-[[5-(1-pyrrolidinyl)-2H-tetrazol-2-yl]methyl]- (9CI) (CA INDEX NAME)



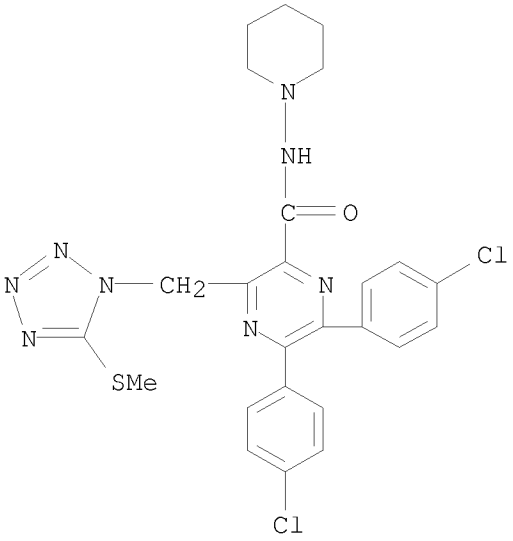
RN 811442-11-2 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-1-piperidinyl-3-[[5-(1-pyrrolidinyl)-1H-tetrazol-1-yl]methyl]- (9CI) (CA INDEX NAME)



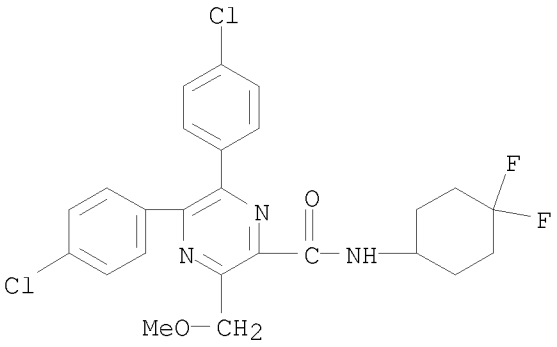
RN 811442-12-3 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[[5-(methylthio)-2H-tetrazol-2-yl]methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



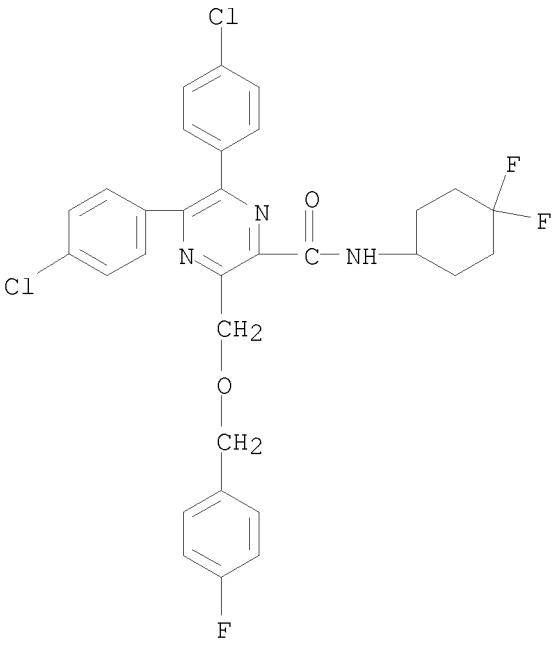
RN 811442-13-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[[5-(methylthio)-1H-tetrazol-1-yl]methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



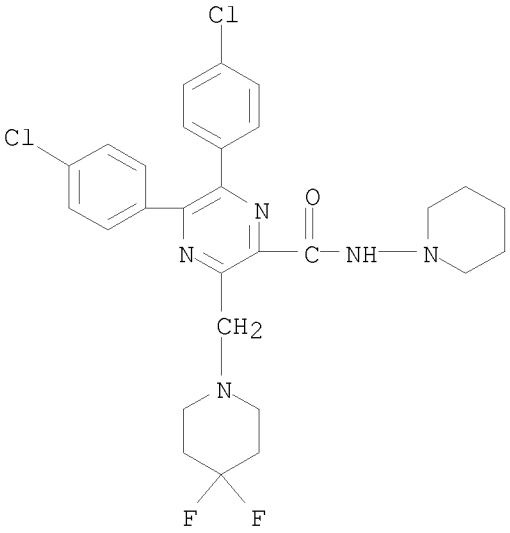
RN 811442-14-5 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-(methoxymethyl)- (9CI) (CA INDEX NAME)



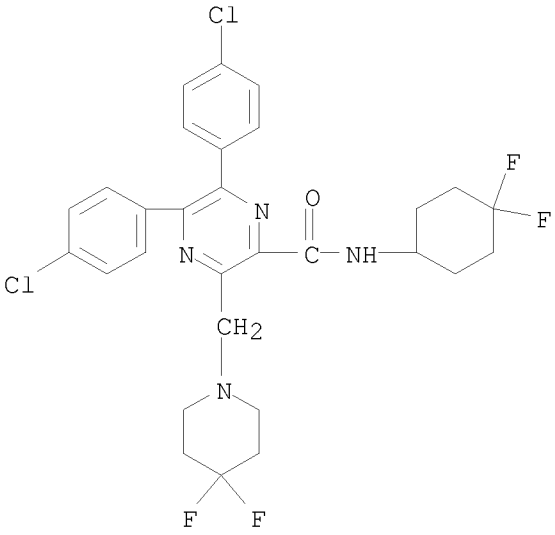

RN 811442-16-7 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-[[(4-fluorophenyl)methoxy]methyl]- (9CI) (CA INDEX NAME)



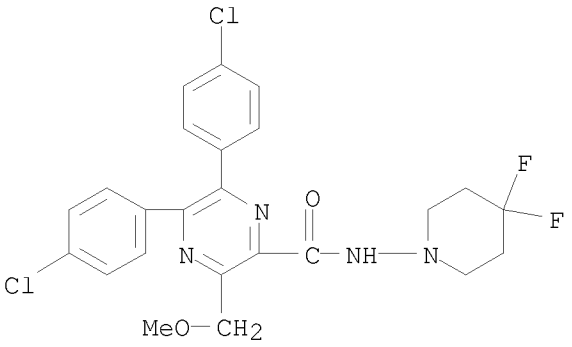

RN 811442-19-0 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[(4,4-difluoro-1-piperidinyl)methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)



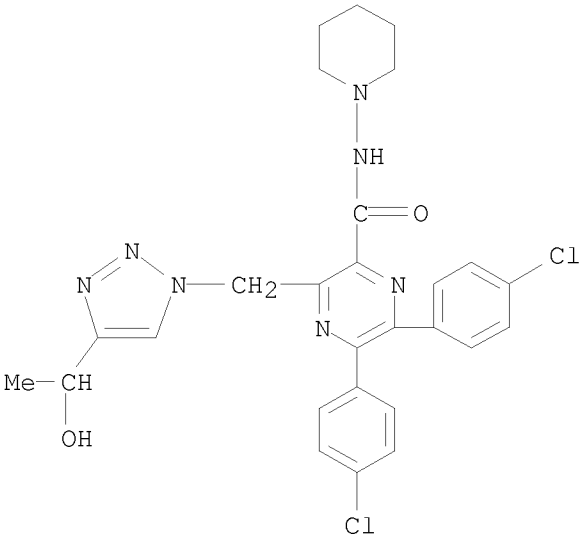
RN 811442-21-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-(4,4-difluorocyclohexyl)-3-[(4,4-difluoro-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



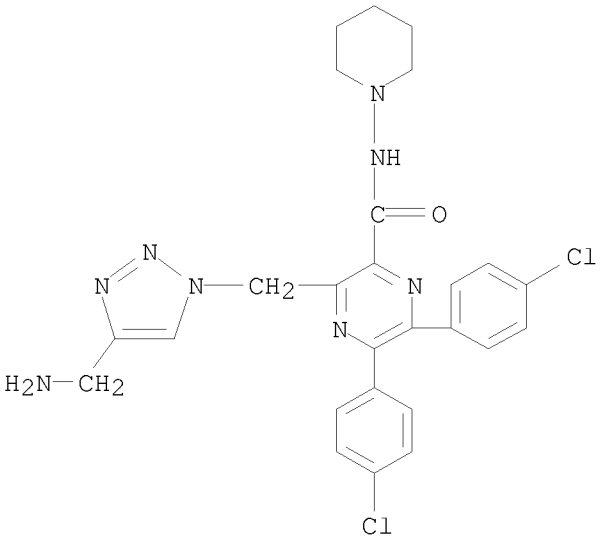
RN 811442-22-5 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-N-(4,4-difluoro-1-piperidinyl)-3-(methoxymethyl)- (9CI) (CA INDEX NAME)



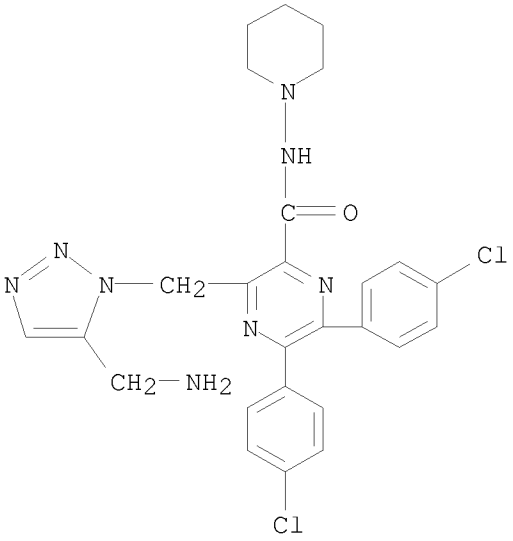

RN 811442-24-7 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-[[4-(1-hydroxyethyl)-1H-1,2,3-triazol-1-yl]methyl]-N-1-piperidinyl- (9CI) (CA INDEX NAME)




RN 811442-25-8 CAPLUS
CN Pyrazinecarboxamide, 3-[[4-(aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)

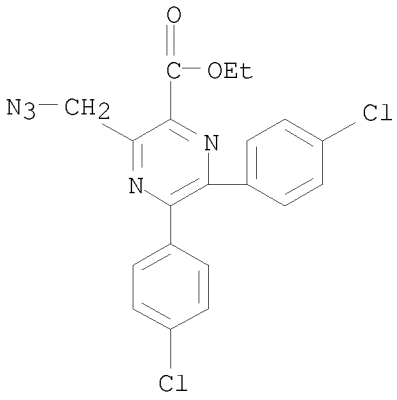


RN 811442-26-9 CAPLUS
CN Pyrazinecarboxamide, 3-[[5-(aminomethyl)-1H-1,2,3-triazol-1-yl]methyl]-5,6-bis(4-chlorophenyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)

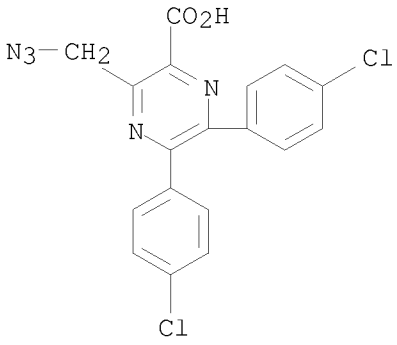


IT 811441-28-8P, Ethyl 3-(azidomethyl)-5,6-bis(4-chlorophenyl)pyrazine-2-carboxylate 811441-29-9P, 3-(Azidomethyl)-5,6-bis(4-chlorophenyl)pyrazine-2-carboxylic acid 811441-30-2P, 3-(Azidomethyl)-5,6-bis(4-chlorophenyl)pyrazine-2-carbonyl chloride 811441-31-3P, 3-(Azidomethyl)-5,6-bis(4-chlorophenyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide 811442-09-8P, 5,6-Bis(4-chlorophenyl)-3-(hydroxymethyl)-N-(piperidin-1-yl)pyrazine-2-carboxamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of 3-substituted 5,6-diarylpyrazine-2-carboxamide and 2-sulfonamide derivs. as CB1 modulators)
RN 811441-28-8 CAPLUS
CN Pyrazinecarboxylic acid, 3-(azidomethyl)-5,6-bis(4-chlorophenyl)-, ethyl

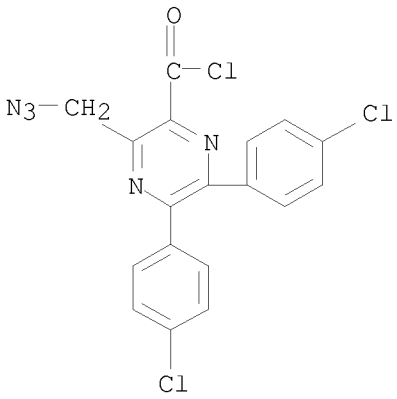
ester (9CI) (CA INDEX NAME)



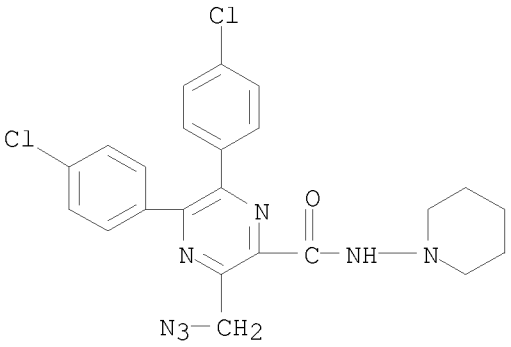
RN 811441-29-9 CAPLUS
CN Pyrazinecarboxylic acid, 3-(azidomethyl)-5,6-bis(4-chlorophenyl)- (9CI) (CA INDEX NAME)



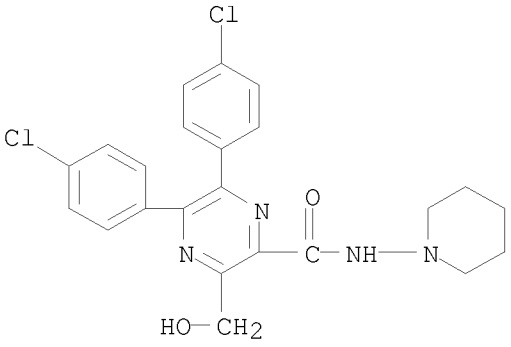
RN 811441-30-2 CAPLUS
CN Pyrazinecarbonyl chloride, 3-(azidomethyl)-5,6-bis(4-chlorophenyl)- (9CI) (CA INDEX NAME)



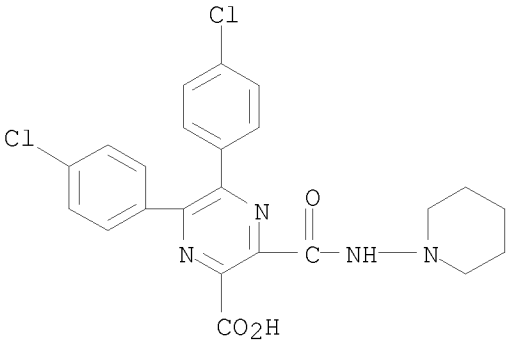
RN 811441-31-3 CAPLUS
CN Pyrazinecarboxamide, 3-(azidomethyl)-5,6-bis(4-chlorophenyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)



RN 811442-09-8 CAPLUS
CN Pyrazinecarboxamide, 5,6-bis(4-chlorophenyl)-3-(hydroxymethyl)-N-1-piperidinyl- (9CI) (CA INDEX NAME)

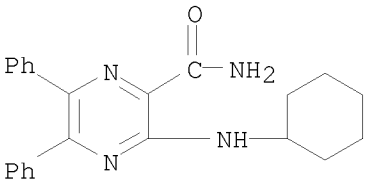


IT 811441-51-7, 5,6-Bis(4-chlorophenyl)-3-[[(piperidin-1-yl)amino]carbonyl]pyrazine-2-carboxylic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3-substituted 5,6-diarylpyrazine-2-carboxamide and 2-sulfonamide derivs. as CB1 modulators)
RN 811441-51-7 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-bis(4-chlorophenyl)-3-[(1-piperidinylamino)carbonyl]- (9CI) (CA INDEX NAME)

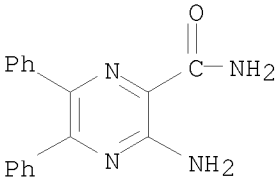


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:205967 CAPLUS
DOCUMENT NUMBER: 142:113926
TITLE: Product class 14: pyrazines
AUTHOR(S): Sato, N.
CORPORATE SOURCE: Germany
SOURCE: Science of Synthesis (2004), 16, 751-844
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Methods for preparing pyrazines are reviewed including cyclization, ring transformation, aromatization and substituent modification.
IT 64344-98-5P 101445-25-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyrazines via cyclization, ring transformation, aromatization and substituent modification)
RN 64344-98-5 CAPLUS
CN Pyrazinecarboxamide, 3-(cyclohexylamino)-5,6-diphenyl- (9CI) (CA INDEX NAME)



RN 101445-25-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 506 THERE ARE 506 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

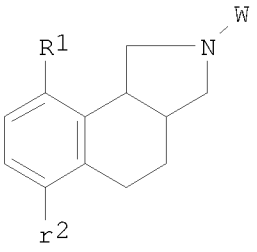
L7 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:102094 CAPLUS
DOCUMENT NUMBER: 126:199575
TITLE: Tricyclic substituted hexahydrobenz[e]isoindole alpha-1 adrenergic antagonists
INVENTOR(S): Meyer, Michael D.; Altenbach, Robert J.; Basha, Fatima Z.; Carroll, William A.; Drizin, Irene; Elmore, Steven W.; Kerwin, James F., Jr.; Lebold, Suzanne A.; Lee, Edmund L.; Sippy, Kevin B.; Tietje, Karin R.; Wendt, Michael D.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 73 pp., Cont.-in-part of U.S. Ser. No. 379,414, abandoned.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5597823 | A | 19970128 | US 1995-463528 | 19950605 |
| IL 116405 | A | 20010913 | IL 1995-116405 | 19951215 |
| CA 2211212 | A1 | 19960801 | CA 1996-2211212 | 19960111 |
| WO 9622992 | A1 | 19960801 | WO 1996-US72 | 19960111 |
| W: AU, CA, JP, KR, MX | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9647457 | A | 19960814 | AU 1996-47457 | 19960111 |
| AU 705283 | B2 | 19990520 | | |
| EP 808318 | A1 | 19971126 | EP 1996-903340 | 19960111 |
| EP 808318 | B1 | 20000628 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| AT 194141 | T | 20000715 | AT 1996-903340 | 19960111 |
| ES 2149451 | T3 | 20001101 | ES 1996-903340 | 19960111 |
| PT 808318 | T | 20001229 | PT 1996-903340 | 19960111 |
| JP 2001504797 | T | 20010410 | JP 1996-522867 | 19960111 |
| GR 3034485 | T3 | 20001229 | GR 2000-402174 | 20000926 |

PRIORITY APPLN. INFO.: US 1995-379414 B2 19950127
US 1995-463528 A 19950605
WO 1996-US72 W 19960111

OTHER SOURCE(S): MARPAT 126:199575
GI



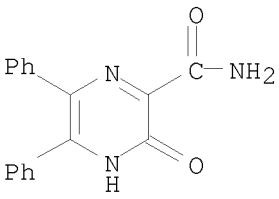

I

AB I (W = tricyclic heterocyclic ring system, e. g. pyrazinothienopyrimidinediones, pyridofuropyrimidinediones, pyrazinothienopyrimidinediones; n = 2-6; R1 and R2 = H, alkoxy, hydroxy, alkyl, halo, carboxy, alkoxycarbonyl) and their pharmaceutically acceptable salts were prepared I are α-1 adrenergic antagonists and useful in the treatment of BPH (benign prostrate hyperplasia). α-1 Antagonist compns. and a method for antagonizing α-1 receptors and treating BPH are also disclosed.

IT 34121-79-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of tricyclic substituted hexahydrobenzisoindoles as alpha-1 adrenergic antagonists)

RN 34121-79-4 CAPLUS

CN Pyrazinecarboxamide, 3,4-dihydro-3-oxo-5,6-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:580282 CAPLUS
DOCUMENT NUMBER: 125:221858
TITLE: Preparation of tricyclic substituted benz[e]isoindoles as α1 adrenergic antagonists
INVENTOR(S): Meyer, Michael D.; Altenbach, Robert J.; Basha, Fatima Z.; Carroll, William A.; Drizin, Irene; Kerwin, James F., Jr.; Lebold, Suzanne A.; Lee, Edmund L.; Elmore, Steven W.; et al.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

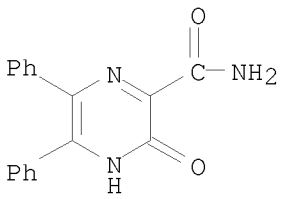
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9622992 | A1 | 19960801 | WO 1996-US72 | 19960111 |
| W: AU, CA, JP, KR, MX | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5597823 | A | 19970128 | US 1995-463528 | 19950605 |
| AU 9647457 | A | 19960814 | AU 1996-47457 | 19960111 |
| AU 705283 | B2 | 19990520 | | |
| EP 808318 | A1 | 19971126 | EP 1996-903340 | 19960111 |
| EP 808318 | B1 | 20000628 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE | | | | |
| AT 194141 | T | 20000715 | AT 1996-903340 | 19960111 |
| JP 2001504797 | T | 20010410 | JP 1996-522867 | 19960111 |
| GR 3034485 | T3 | 20001229 | GR 2000-402174 | 20000926 |
| PRIORITY APPLN. INFO.: | | | US 1995-379414 A | 19950127 |
| | | | US 1995-463528 A | 19950605 |
| | | | WO 1996-US72 W | 19960111 |

OTHER SOURCE(S): MARPAT 125:221858
GI

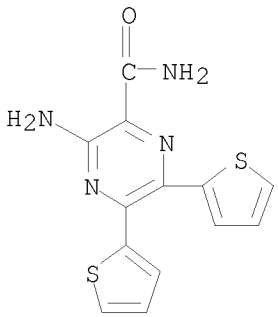
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = H, alkoxy, OH, etc.; W = tricyclic heterocyclic ring system; n = 2-6] and their salts, useful in the treatment of benign prostatic hypertrophy (BPH), were prepared Thus, reaction of urea II with benz[e]isoindole III in the presence of (iPr)2NEt in DMSO afforded the desired product cis-IV.HCl which showed pA2 of 8.37 for inhibition of phenylepherine(PE)-induced contraction of rat vas.
IT 34121-79-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tricyclic substituted benz[e]isoindoles as α1 adrenergic antagonists)

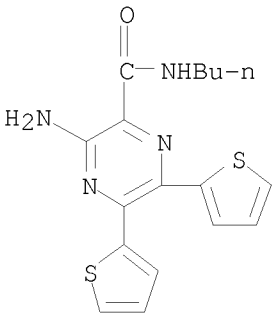
RN 34121-79-4 CAPLUS
CN Pyrazinecarboxamide, 3,4-dihydro-3-oxo-5,6-diphenyl- (9CI) (CA INDEX NAME)



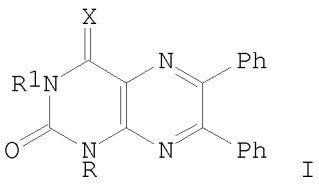
L7 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:466654 CAPLUS
DOCUMENT NUMBER: 125:157774
TITLE: Anthelmintic activity of 6,7-diarylpteridines
AUTHOR(S): Ochoa, Carmen; Rodriguez, Juan; Lopez Garcia, Maria Luz; Martinez, Antonio Ramon; Martinez, Maria Mercedes
CORPORATE SOURCE: Fac. Farm., Univ. Complutense, Madrid, E-28006, Spain
SOURCE: Arzneimittel-Forschung (1996), 46(6), 643-648
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Cantor
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In search for new anthelmintic compds., some 6,7-diaryl-pteridines were synthesized from the corresponding diaminopyrimidines and aromatic aldehydes. Their anthelmintic activity was tested in vitro against Caenorhabditis elegans and Heligmosomoides polygyrus and in vivo against Trichinella spiralis. Structure-activity relationships are discussed.
IT 180603-98-9P 180603-99-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(anthelmintic activity and preparation of diarylpteridines)
RN 180603-98-9 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-di-2-thienyl- (9CI) (CA INDEX NAME)



RN 180603-99-0 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-butyl-5,6-di-2-thienyl- (9CI) (CA INDEX NAME)



L7 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:119534 CAPLUS
DOCUMENT NUMBER: 106:119534
TITLE: Pteridines. LXXVIII. Reactions and properties of 4-thiolumazine derivatives
AUTHOR(S): Lutz, Herman; Pfleiderer, Wolfgang
CORPORATE SOURCE: Fak. Chem., Univ. Konstanz, Konstanz, D-7750, Fed. Rep. Ger.
SOURCE: Croatica Chemica Acta (1986), 59(1), 199-220
CODEN: CCACAA; ISSN: 0011-1643
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



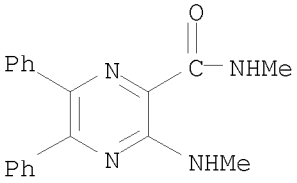
I

AB The 4-thioxo function in the 6,7-diphenyl-4-thiolumazines I (X = S, R, R1 = H, Me) showed easy displacement by nucleophiles under mild conditions. Special structural and electronic features became obvious with I (X = S, R = H, R1 = Me), which reacted analogously to I (X = S, R = R1 = Me) with amines to I (X = NH, NMe, NEt, NBu, NNHPh, NHHMe, NNMePh). The latter compds. are very light-sensitive and react by photooxidn. to give I (X = O). Nucleophilic displacement by alkoxides under HgBr2 catalysis yielded the unusual 4,4-di-O-alkyl acetals I [X = (OMe)2, OCH2CH2O]. The acetal function is prone to easy substitution by C-H acidic compds., giving I [X = C(CN)2] from I [X = (OMe)2].

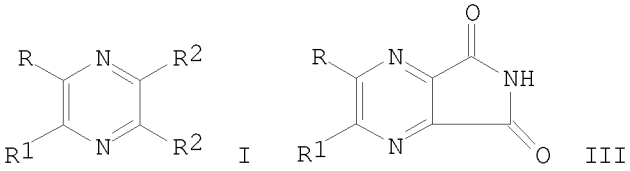
IT 25472-83-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 25472-83-7 CAPLUS

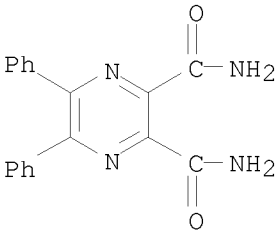
CN Pyrazinecarboxamide, N-methyl-3-(methylamino)-5,6-diphenyl- (8CI, 9CI) (CA INDEX NAME)



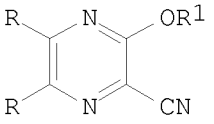
L7 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:68939 CAPLUS
DOCUMENT NUMBER: 96:68939
ORIGINAL REFERENCE NO.: 96:11329a,11332a
TITLE: Synthesis of pyrazinedicarboximides from diaminomaleonitrile
AUTHOR(S): Tsuda, Tadataka; Fujishima, Katsuhiro; Ueda, Hiroo
CORPORATE SOURCE: Coll. Agric., Univ. Osaka Prefect., Osaka, 591, Japan
SOURCE: Agricultural and Biological Chemistry (1981), 45(9), 2129-30
CODEN: ABCHA6; ISSN: 0002-1369
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 96:68939
GI



AB Hydrolysis of pyrazines I (R = H, Me, Ph, 4-ClC6H4, 3,4-Cl2C6H3, 4-MeOC6H4; R1 = H, Me, Ph; R2 = CN), prepared from diaminomaleonitrile, followed by esterification gave I (R2 = CO2Me)(II). Amidn. of II with NH3 followed by intramol. cyclocondensation gave the title compds. (III). II (R = Ph, R1 = H, R2 = CO2Me) showed bactericidal activity superior to that of phenazine oxide.
IT 80356-91-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of, pyridinedicarboximide from)
RN 80356-91-8 CAPLUS
CN 2,3-Pyrazinedicarboxamide, 5,6-diphenyl- (CA INDEX NAME)



L7 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:586294 CAPLUS
DOCUMENT NUMBER: 93:186294
ORIGINAL REFERENCE NO.: 93:29698h,29699a
TITLE: One-step preparation of 3-alkoxypyrazine-2-carbonitriles from pyrazine-2,3-dicarbonitriles and related reactions
AUTHOR(S): Kojima, Takakazu; Nagasaki, Fumihiko; Ohtsuka, Yozo
CORPORATE SOURCE: Fine Chem. Res. Lab., Nippon Soda Co. Ltd., Odawara, 250-02, Japan
SOURCE: Journal of Heterocyclic Chemistry (1980), 17(3), 455-9
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 93:186294
GI



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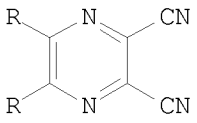
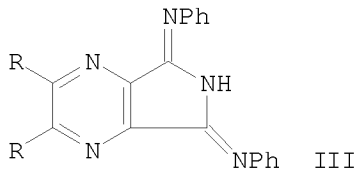
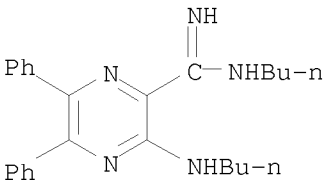


II



III

AB Disubstituted alkoxypyrazinecarbonitriles I (R = Ph, H, 1,8-C10H6, 9,10-phenanthrenediyl; R1 = alkyl) were prepared from the pyrazinedicarbonitriles II by direct substitution with alcs. Treatment of II with amines gave either pyrrolopyrazines III (R = H, Ph) or substitution products. In a low temperature range, II afforded imidates and related compds. The preference among these reactions depended on the 5,6-substituents and on the reaction conditions.
IT 75018-16-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 75018-16-5 CAPLUS
CN Pyrazinecarboximidamide, N-butyl-3-(butylamino)-5,6-diphenyl- (9CI) (CA INDEX NAME)

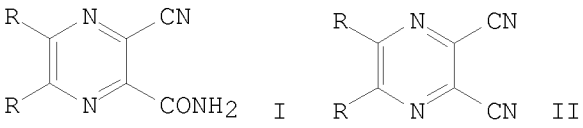



L7 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:446712 CAPLUS
DOCUMENT NUMBER: 93:46712

ORIGINAL REFERENCE NO.: 93:7730h,7731a
TITLE: Pyrazinecyanocarboxamides
INVENTOR(S): Genda, Yoshikazu; Tomita, Nobuo; Ito, Masaru; Kano, Saburo
PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

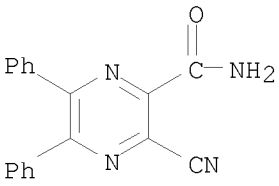
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 54154776 | A | 19791206 | JP 1978-63655 | 19780527 |
| JP 61056230 | B | 19861201 | | |

PRIORITY APPLN. INFO.: JP 1978-63655 A 19780527
GI

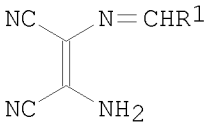


I II

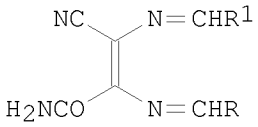
AB Title compds. I (R = H, Me, Ph) were prepared by treating II with HCl and AcOH. Thus, stirring a mixture of 5 g II, 40 mL 35% HCl, and 5 mL AcOH for 3 h 15 min at 30-5° gave 86.1% I (R = H).
IT 66371-68-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 66371-68-4 CAPLUS
CN Pyrazinecarboxamide, 3-cyano-5,6-diphenyl- (9CI) (CA INDEX NAME)



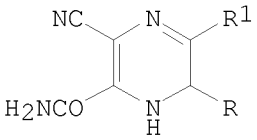
L7 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1980:41887 CAPLUS
DOCUMENT NUMBER: 92:41887
ORIGINAL REFERENCE NO.: 92:6993a,6996a
TITLE: Chemistry of diaminomaleonitrile. 5. Dihydropyrazine synthesis
AUTHOR(S): Ohtsuka, Yozo; Tohma, Eiko; Kojima, Sigeru; Tomita, Nobuo
CORPORATE SOURCE: Sagami Chem. Res. Cent., Sagamihara, 229, Japan
SOURCE: Journal of Organic Chemistry (1979), 44(26), 4871-6
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 92:41887
GI



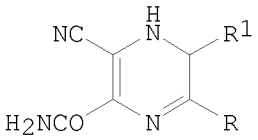
I



II



III



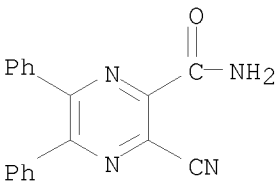
IV

AB Condensation of RCHO (R = optionally substituted Ph) with Schiff bases I (R1 = optionally substituted Ph, CHMe2) in the presence of NEt3 <20° is accompanied by regiospecific hydration of the nitrile groups to give 3-cyanoacrylamide derivs. II, which cyclize readily into 1,2-dihydropyrazines III and IV. The substituent effect on the product ratio is examined, and the reaction mechanism is discussed in terms of a new general reaction pattern of diaminomaleonitrile derivative Reactions of III and IV by oxidation, reduction, hydantoin formation with isocyanates, and cyanoethylation are also reported.

IT 66371-68-4P 71871-19-7P 71871-20-0P
71871-22-2P 71871-23-3P 71871-24-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

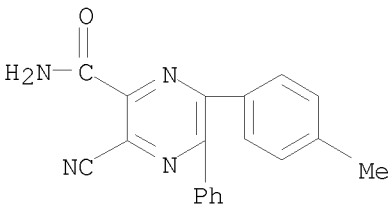
RN 66371-68-4 CAPLUS

CN Pyrazinecarboxamide, 3-cyano-5,6-diphenyl- (9CI) (CA INDEX NAME)



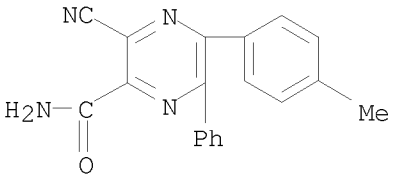
RN 71871-19-7 CAPLUS

CN Pyrazinecarboxamide, 3-cyano-6-(4-methylphenyl)-5-phenyl- (9CI) (CA INDEX NAME)

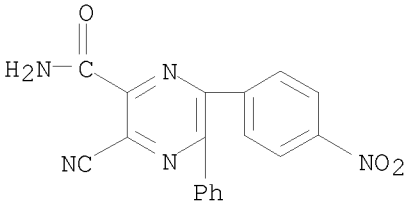


RN 71871-20-0 CAPLUS

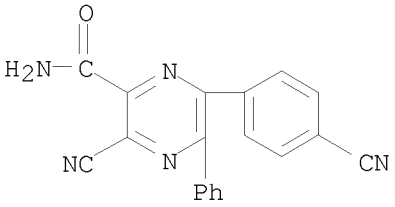
CN Pyrazinecarboxamide, 3-cyano-5-(4-methylphenyl)-6-phenyl- (9CI) (CA INDEX NAME)



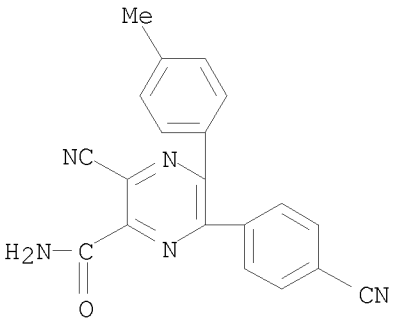
RN 71871-22-2 CAPLUS
CN Pyrazinecarboxamide, 3-cyano-6-(4-nitrophenyl)-5-phenyl- (9CI) (CA INDEX NAME)



RN 71871-23-3 CAPLUS
CN Pyrazinecarboxamide, 3-cyano-6-(4-cyanophenyl)-5-phenyl- (9CI) (CA INDEX NAME)



RN 71871-24-4 CAPLUS
CN Pyrazinecarboxamide, 3-cyano-6-(4-cyanophenyl)-5-(4-methylphenyl)- (9CI) (CA INDEX NAME)

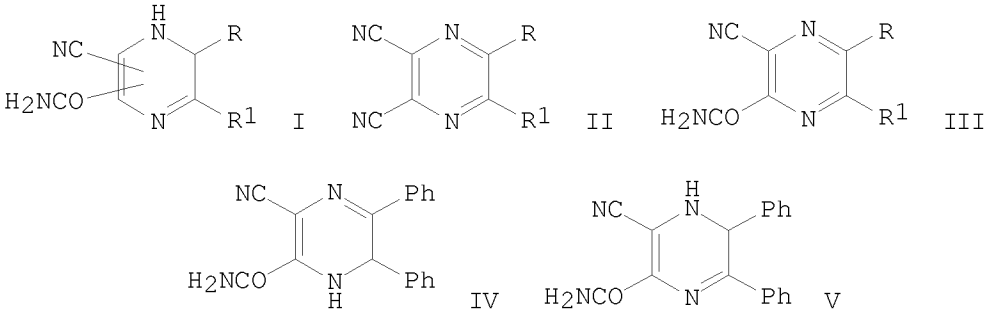


L7 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:171793 CAPLUS
DOCUMENT NUMBER: 88:171793
ORIGINAL REFERENCE NO.: 88:27075a,27078a
TITLE: 1,2-Dihydropyrazine derivatives
INVENTOR(S): Ohtsuka, Yozo; Ito, Masaru; Tomita, Nobuo

PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan; Sagami Chemical Research Center
SOURCE: Ger. Offen., 48 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2736230 | A1 | 19780216 | DE 1977-2736230 | 19770811 |
| JP 53022529 | A | 19780302 | JP 1976-96020 | 19760813 |
| JP 57045260 | B | 19820927 | | |

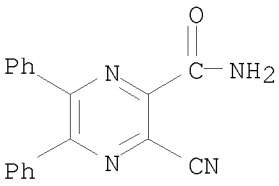
PRIORITY APPLN. INFO.: JP 1976-96020 A 19760813
GI



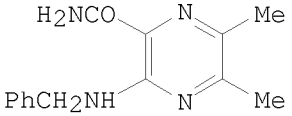

AB Title compds. (I; R, R1 = Ph, condensed aromatic, or heterocyclic groups), fast yellow dyes showing a green to yellow luminescence, are prepared (a) by condensing RCH:NC(CN):C(CN)NH2 with R1CHO in the presence of base to give RCH:NC(CN):C(CONH2)N:CHR1, followed by ring closure, or (b) by selective hydrolysis of II to III, followed by selective reduction Thus, reaction of PhCH:NC(CN):C(CN)NH2 [56029-18-6] with PhCHO [100-52-7] in EtOH containing Et3N gave PhCH:NC(CN):C(CONH2)N:CHPh [66371-72-0], which was cyclized by heating with Me2SO to form a mixture of IV [66371-73-1] and V [66371-74-2]. The IV-V mixture, resolvable by fractional recrystn., showed (Japanese standard test K 5101) a brilliant greenish yellow tone, solvent stability 4-5 (1 lowest, 5 highest), and water stability 5, and lightfastness (Fade-O-meter) 7-8.

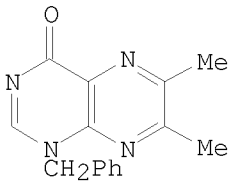
IT 66371-68-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and selective reduction of)

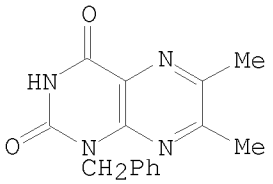
RN 66371-68-4 CAPLUS
CN Pyrazinecarboxamide, 3-cyano-5,6-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:552132 CAPLUS
DOCUMENT NUMBER: 87:152132
ORIGINAL REFERENCE NO.: 87:24075a,24078a
TITLE: Amidinoacetamides in the synthesis of pyrazines and pteridines
AUTHOR(S): Keir, William F.; MacLennan, Alexander H.; Wood, Hamish C. S.
CORPORATE SOURCE: Paisley Coll. Technol., Paisley, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1977), (11), 1321-5
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 87:152132
GI


I

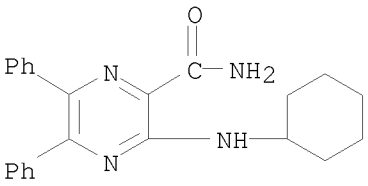

II


III

AB Cyclocondensation of 2-(substituted amidino)-2-aminoacetamides with 1,2-dicarbonyl compds. gave 3-(substituted amino)-pyrazine-2-carboxamides which with one-carbon units gave 1-substituted pteridin-4(1H-)-ones and -2,4-(1H)-diones. E.g., PhCH2NHC(:NH)CH(NH2)CONH2.HCl with biacetyl gave 80% pyrazine I which with HCO2H and ClCO2Et gave 60% pteridinone II and 59% pteridinedione III, resp.

IT 64344-98-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation reaction of, with diethoxydimethylformamide)

RN 64344-98-5 CAPLUS
CN Pyrazinecarboxamide, 3-(cyclohexylamino)-5,6-diphenyl- (9CI) (CA INDEX NAME)

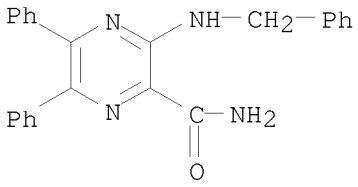


IT 64344-96-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation reactions of, with formic acid and Et chloroformate)

RN 64344-96-3 CAPLUS

CN Pyrazinecarboxamide, 5,6-diphenyl-3-[(phenylmethyl)amino]- (9CI) (CA INDEX NAME)



L7 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1976:593017 CAPLUS

DOCUMENT NUMBER: 85:193017

ORIGINAL REFERENCE NO.: 85:30879a,30882a

TITLE: Nucleosides, XIX. Synthesis, properties and chemical behavior of 1(3)-methyl-6,7-diphenyl-3(1)-(β-D-ribofuranosyl)lumazine derivatives

AUTHOR(S): Kobayashi, Kiyotaka; Pfleiderer, Wolfgang

CORPORATE SOURCE: Fachber. Chem., Univ. Konstanz, Konstanz, Fed. Rep. Ger.

SOURCE: Chemische Berichte (1976), 109(9), 3194-207
CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: German

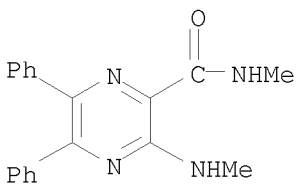
GI For diagram(s), see printed CA Issue.

AB Ribofuranosyllumazine I (R = R2, R1 = Me, R3-R5 = H) (II) was prepared by coupling 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose (III) with O-trimethylsilyl derivative of I (R = H, R1 = Me) followed by alkaline hydrolysis.
Similarly I (R = Me, R1 = R2, R3-R5 = H) (IV) was prepared from I (R = Me, R1 = H) and III. Isopropylidenation of II and IV gave I (R = R2, R1 = H, R4R5 = CMe2) (V) and I (R = H, R1 = R2, R4R5 = CMe2) (VI). In the alkaline hydrolysis of IV-VI the nucleophilic attack occurred at the CO group at C-2 with cleavage of the pyrimidine ring and formation of the corresponding 3-amino-5,6-diphenyl-2-pyrazinecarboxamides.

IT 25472-83-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with ethyl chloroformate)

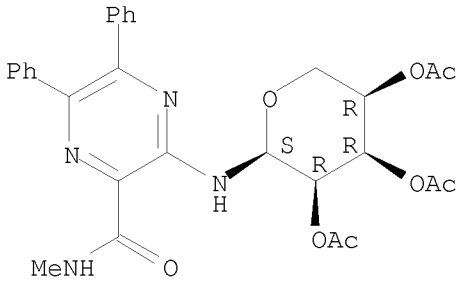
RN 25472-83-7 CAPLUS

CN Pyrazinecarboxamide, N-methyl-3-(methylamino)-5,6-diphenyl- (8CI, 9CI) (CA INDEX NAME)



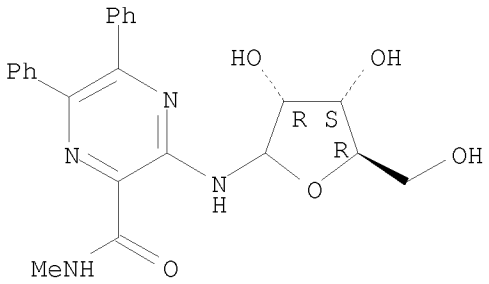
IT 60980-87-2P 60980-97-4P 60980-98-5P
60980-99-6P 60981-00-2P 60981-01-3P
60981-02-4P 60981-03-5P 60981-04-6P
60981-05-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 60980-87-2 CAPLUS
CN Pyrazinecarboxamide, N-methyl-5,6-diphenyl-3-[(2,3,4-tri-O-acetyl-α-D-ribopyranosyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

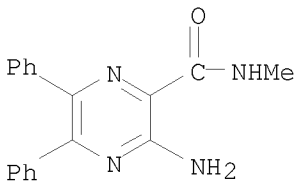



RN 60980-97-4 CAPLUS
CN Pyrazinecarboxamide, N-methyl-5,6-diphenyl-3-(D-ribofuranosylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

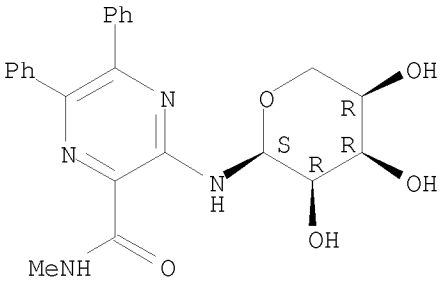



RN 60980-98-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-methyl-5,6-diphenyl- (9CI) (CA INDEX NAME)



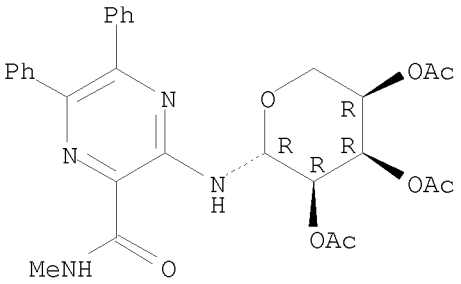

RN 60980-99-6 CAPLUS
CN Pyrazinecarboxamide, N-methyl-5,6-diphenyl-3-(α-D-ribopyranosylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



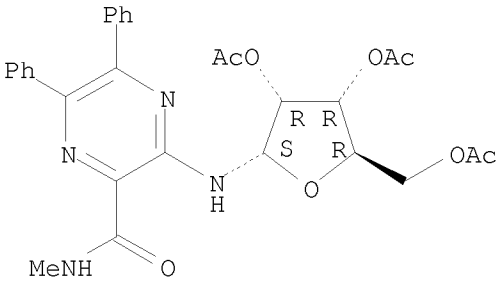

RN 60981-00-2 CAPLUS
CN Pyrazinecarboxamide, N-methyl-5,6-diphenyl-3-[(2,3,4-tri-O-acetyl-β-D-ribopyranosyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



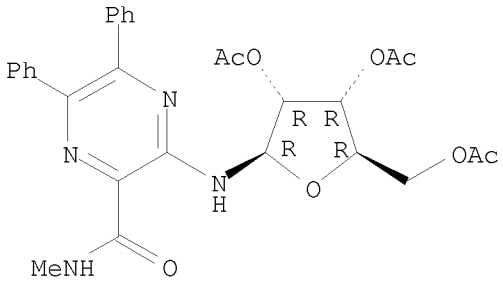

RN 60981-01-3 CAPLUS
CN Pyrazinecarboxamide, N-methyl-5,6-diphenyl-3-[(2,3,5-tri-O-acetyl-α-D-ribofuranosyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



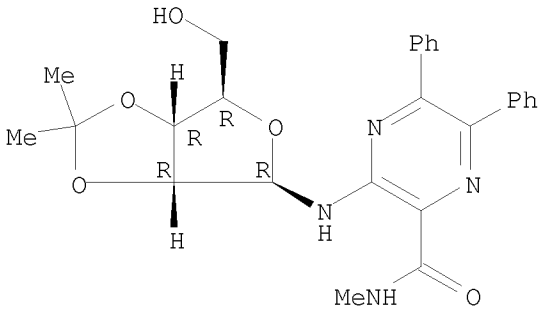

RN 60981-02-4 CAPLUS
CN Pyrazinecarboxamide, N-methyl-5,6-diphenyl-3-[(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



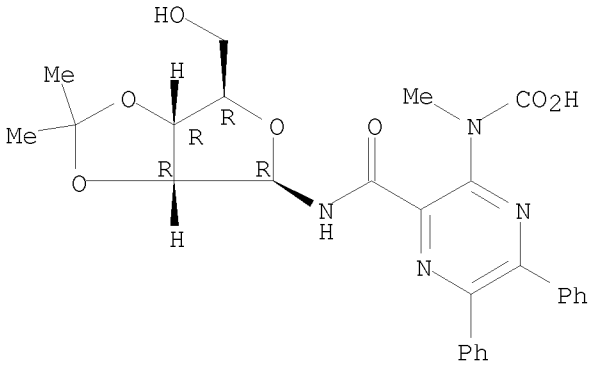
RN 60981-03-5 CAPLUS
CN Pyrazinecarboxamide, N-methyl-3-[[2,3-O-(1-methylethylidene)-β-D-ribofuranosyl]amino]-5,6-diphenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



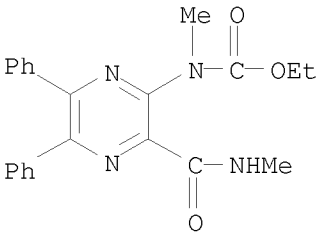
RN 60981-04-6 CAPLUS
CN Carbamic acid, methyl[3-[[[2,3-O-(1-methylethylidene)-β-D-ribofuranosyl]amino]carbonyl]-5,6-diphenylpyrazinyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

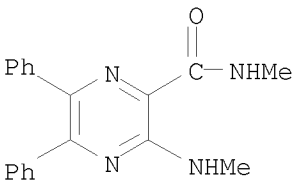


● Na

RN 60981-05-7 CAPLUS
CN Carbamic acid, methyl[3-[(methylamino)carbonyl]-5,6-diphenylpyrazinyl]-, ethyl ester (9CI) (CA INDEX NAME)

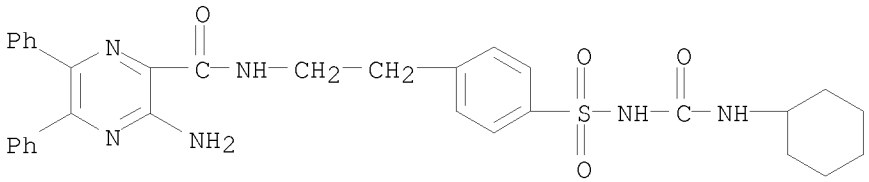


L7 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:518287 CAPLUS
DOCUMENT NUMBER: 75:118287
ORIGINAL REFERENCE NO.: 75:18673a,18676a
TITLE: Alkylation of 4-oxopteridines
AUTHOR(S): Neiman, Zohar; Bergmann, Felix; Meyer, Amatzya Y.
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel
SOURCE: Chem. Biol. Pteridines, Proc. Int. Symp., 4th (1970), Meeting Date 1969, 29-34. Editor(s): Iwai, K. Int. Acad. Print. Co.: Tokyo, Japan.
CODEN: 23BVAJ
DOCUMENT TYPE: Conference
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB 4-Pteridin-one (I), 6,7-dimethyl-4-pteridinone (II), and 6,7-diphenyl-4-pteridinone (III) were alkylated exclusively in the pyrimidine ring by MeI-DMF to yield the corresponding 1,3-dimethyl-4-oxopteridinium salts IV, V, and VI in 10%, 50% and 50% yield, resp. The pyrimidine ring of these methylation products was cleaved readily by hot 2N NaOH to yield the corresponding pyrazines. Reduction of IV, V, and VI with NaBH4 yielded the corresponding derivs. of 1,2-dihydropteridine. The reaction path to IV, V, and VI was studied by paper chromatog., and related with charge ds. calculated by the HMO and the SCF-Pariser-Pople-Parr methods.
IT 25472-83-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 25472-83-7 CAPLUS
CN Pyrazinecarboxamide, N-methyl-3-(methylamino)-5,6-diphenyl- (8CI, 9CI) (CA INDEX NAME)



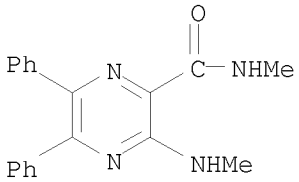
L7 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:488570 CAPLUS
DOCUMENT NUMBER: 75:88570
ORIGINAL REFERENCE NO.: 75:14029a,14032a
TITLE: New oral antidiabetic drugs. I
AUTHOR(S): Ambrogi, V.; Bloch, Konrad; Daturi, S.; Griggi, P.; Logemann, W.; Parenti, M. A.; Rabini, T.; Tommasini, R.

CORPORATE SOURCE: Ist. Carlo Erba Ric. Ter., Milan, Italy
SOURCE: Arzneimittel-Forschung (1971), 21(2), 200-4
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB All of 20 new pyrazinecarboxamidoethylphenylnesulfonylureas had hypoglycemic activity in mice, and 19 were active in rats; in rats N - (4 - [β - (5 -methylpyrazine -2-carboxamido)ethyl]phenylsulfonyl)-N'-cyclohexylurea (I) was the most active producing a hypoglycemic activity of 46% at 1.5 mg/kg orally. 4-(4-[β-(5-Methylpyrazine-2-carboxamido)ethyl]phenylsulfonyl)-1,1 - hexamethylenesemicarbazide (II), the only pyrazinecarboxamidoethylphenylsulfonylsemicarbazide tested, was as effective as I at the same dose. Neither of the 2 pyrazinecarboxamidocycloalkylphenylsulfonylureas tested had antidiabetic activity in mice or rats. The sulfonamide were synthesized by reacting pyrazine-, pyridazine-, or pyrimidinecarboxamidobenzenesulfonamides with cyclohexyl isocyanate. Intermediate benzenesulfonamides were prepared by acylation of p-(β-aminoethyl)benzenesulfonamide. II was prepared from Me-4-[β-(5-methylpyrazine-2-carboxamido)ethyl] phenylsulfonylcarbamate and 1-aminohexamethyleneimine.
IT 33282-78-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 33282-78-9 CAPLUS
CN Urea, 1-[[p-[2-(3-amino-5,6-diphenylpyrazinecarboxamido)ethyl]phenyl]sulfonyl]-3-cyclohexyl- (8CI) (CA INDEX NAME)



L7 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1970:55408 CAPLUS
DOCUMENT NUMBER: 72:55408
ORIGINAL REFERENCE NO.: 72:10145a,10148a
TITLE: Reduction of quaternary pteridines and purines by sodium borohydride
AUTHOR(S): Neiman, Zohar
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel
SOURCE: Journal of the Chemical Society [Section] C: Organic (1970), (1), 91-4
CODEN: JSOOAX; ISSN: 0022-4952
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 72:55408
AB In the 3,4-dihydro-1,3-dimethyl-5,6-diphenyl-4-oxopteridinium cation, and in the 1,3-dimethyl-8-phenylhypo-xanthinium cation, position 2 of the pyr imidine ring is reduced by NaBH4. The analogous reaction at position 8 was observed for the 7,9-dimethylhypoxanthinium cation. The structures assigned to the reduction products are supported by spectral data and by degradation reactions.
IT 25472-83-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 25472-83-7 CAPLUS

CN Pyrazinecarboxamide, N-methyl-3-(methylamino)-5,6-diphenyl- (8CI, 9CI) (CA INDEX NAME)




L7 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1968:436172 CAPLUS
DOCUMENT NUMBER: 69:36172
ORIGINAL REFERENCE NO.: 69:6762h,6763a
TITLE: (3-Amino-2-pyrazinecarbonyl)guanidines
INVENTOR(S): Cragoe, Edward J., Jr.
PATENT ASSIGNEE(S): Merck and Co., Inc.
SOURCE: U.S., 26 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 3313813 | | 19670411 | US 1963-313315 | 19621030 |
| DE 1795438 | | | DE | |

GI For diagram(s), see printed CA Issue.

AB Title compds. I are prepared from II, III, and IV. Thus, 3318 g. SO2Cl2 is added in 30 min. to 765 g. Me 3-amino-2-pyrazinecarboxylate in 5.1 C6H6; the mixture is agitated 1 hr., refluxed 5 hrs., and agitated overnight to give 724 g. Me 3-amino-5,6-dichloropyrazinecarboxylate (V), m. 233-4° (MeCN). A mixture of 100 g. V. and 1.1 Me2SO is heated to 65° and NH3 gas is introduced into the mixture in 45 min. at 65-70°; the mixture is cooled to 10° and NH3 is introduced in 1.25 hrs. to give 91.5% Me 3,5-diamino-6-chloropyrazinecarboxylate, m. 212-13° (MeCN). Also prepared, by known methods are the following II (X, Y, Z, and m.p. given): MeO, NH2, H, 252-4° (decomposition); MeO, NH2, Br, 217-19°; MeO, NH2, iodine, 200-2°; MeO, PhNH, Cl, 171.5-73°; MeO, p-ClC6H4NH, Cl, 207-8°; MeO, Me2N, Cl, 145.5-6.5°; MeO, MeS, Cl, 214-16°; MeO, MeSO, Cl, 237.5-40.5° (decomposition); MeO, OH, Cl, .apprx.245° (decomposition); MeO, OH, H, 220-60° (decomposition); MeO, NH2,H, 252-4° (decomposition); MeO, Me2N, H, 242.5-3.5°; MeO, MeO, H, 205.5-7.5°; MeO, PhCH2NH, H, 157-8°; MeO, MeO, MeO, Cl, 255-7°; MeO, MeS, Cl, 212-14°; MeO, SH, Cl, 207-8° (decomposition); MeO,EtO, Cl, 123-5°; MeO, H, Me, 138.5-40.5°; MeO, Cl, Me, 176.5-9.5°; MeO, Me2N, Me, 108.5-10.5°; MeO, Me, H, 165-7°; MeO, Me, Br, 179-81°; NH2, H, Et, 165.5-8.5°; OH, H, Et, 149-52°; MeO, H, Et, 85-7.5°; OH, cyclohexyl, H, 182.5-3.5°; MeO, cyclohexyl, H, 173-4.5°; NH2, H, cyclohexyl, -; OH, H, cyclohexyl, -; MeO, H, cyclohexyl, 126.5-8.0°; NH2, H, cyclopropyl, 185.5-7.5°; OH, H, cyclopropyl, 169-72°; MeO, H, cyclohexyl, 112.5-14.5°; MeO, Ph, H, 231-2°; MeO, H, Ph, 140-1°; MeO, Cl, Ph, 187.5-91.5°; MeO, Ph, Br, 217-21°; OH, H, p-ClC6H4, 213-15°; MeO, H, p-ClC6H4, 181.5-3.5°; MeO, Cl, Ph,

187.5-90.5°; MeO, Me2N, Ph, 167-9.5°; MeO, H, Cl, 142° (decomposition); MeO, MeHN, Cl, 221-2°; MeO, EtNH, Cl, 149-50°; MeO, PrNH, Cl, 138-40°; MeO, iso-PrNH, Cl, 125.5-6.5°; MeO, CH2:CHCH2NH, Cl, 105-6.5°; MeO, BuNH, Cl, 140-2°; MeO, sec-BuNH, Cl, 106-8°; MeO, iso-BuNH, Cl, 113.5-15.5°; MeO, tert-BuNH, Cl, 98-108°; MeO, Me(CH2)4NH, Cl, 100.5-2.5°; MeO, BuCHMeNH, Cl, -; MeO, Et2CHNH, Cl, -; MeO, Me(CH2)5NH, Cl, 72.5-5.5°; MeO, cyclopropylmethylamino, Cl, 132-3°; MeO, cyclopropylamino, Cl, 167-9°; MeO, cyclopentylamino, Cl, 119.5-21.5°; MeO, PhCH2NH, Cl, 157-8°; MeO, p-MeC6H4CH2NH, Cl, 112.5-14.5°; MeO, o-FC6H4CHNH, Cl, 171-4°; MeO, p-ClC6H4CH2NH, Cl, 136-7°; MeO, PhCH2CH2NH, Cl, 115-19°; MeO, F3CCH2NH, Cl, 153-4°; MeO, F3CCH2CH2NH, Cl, 124.5-5.5°; MeO, HOCH2CH2NH, Cl, 155-7°; MeO, HOCH2(CHOH)4CH2NH, Cl, 172-5°; MeO, H2NCH2CH2NH, Cl, 265°; MeO, Me2NCH2CH2NH, Cl, 257°; MeO, 4-pyridylmethylamino, Cl, 95-7°; Me, 2-furylmethylamino, Cl, 148-9°; MeO, MeEtN, Cl, 102-4°; MeO, MePrN, Cl, 83.5-5.5°; MeO, iso-PrMeN, Cl, 75.5-7.5°; MeO, Me(CH2:CHCH2)N, Cl, 90.5-2°; MeO, MeBun, Cl, 59.5-61.5°; MeO, Et2N, Cl, 99-101°; MeO, EtPrN, Cl, -; MeO, iso-PrEtN, Cl, -; MeO, Et(CH2:CHCH2)N, Cl, -; MeO, EtBun, Cl, 77.5-9.5°; Me, Pr2N, Cl, 68.5-71.5°; MeO, PrBuN, Cl, -; MeO, 1-pyrrolidinyl, Cl, 168-71°; MeO, hexamethylenimino, Cl, 109-11°; MeO, 4-methylpiperazino, Cl, 186-8°; MeO, MeNHNH, Cl, 136.5-8°; MeO, Me2NCH2CH2O, Cl, 134.5-6.5°; NH2, H, Cl, 227-30°; OH, H, MeSO2, 239-42° (decomposition). p-Methylbenzylamine is treated with H2NC(:NH)SMe.0.5H2SO4 to give 28% p-MeC6H4CH2NHC(:NH)NH2HCl, m. 153-5°. Similarly prepared are Me(PhCH2)NC(:NH)NH2.HCl, m. 122.5-5.5°, and the following RNHC(:NH)NH2.HCl (R and m.p. given): o-ClC6H4CH2, 131-6°; p-ClC6H4CH2, 162.5-4.5°; p-MeOC6H4CH2, 132-7°; 2,4-Me2C6H3CH2, 105-15°; 2,4-Cl2C6H3CH2, 145-8°; 3,4-Cl2C6H3CH2, 153-7°; PhCH2CH2, 135-8°; PhCH2, 175-8°. 5,6-Diaminouracil-HCl (17.9 g.) is treated at 60° with 14.9 g. cyclohexylglyoxal-0.5H2O to give 7.5 g. 7-cyclohexyllumazine [III (X = H, Y = cyclohexyl)], m. 229-31°, which is hydrolyzed to give II (X = OH, Y = cyclohexyl, Z = H). Similarly prepared are (m.p. given): III (X = Me, Y = Ph) [or III (X = Me, Y = Me)], 281.5-2.5°; III (X = Ph, Y = Me) [or III (X = Me, Y = Ph) [sic], 254.5-5.5°; II (X = OH, Y = Ph, Z = Me) [or II (X = OH, Y = Me, Z = Ph)], 193.5-4.5°; II (X = OH, Y = Me, Z = Ph) [or II (X = OH, Y = Ph, Z = Me)] [sic], 155-6°. II (X = MeO, Y = Ph, Z = Me) [or II (X = MeO, Y = Me, Z = Ph)] (m. 163-4°) and II (X = MeO, Y = Me, Z = Ph) [or II (X = MeO, Y = Ph, Z = Me)][sic] (m. 162.5-3.5°) are prepared by esterification. Methyl 3-isopropylidenamino-6-anilino-2-pyrazinecarboxylate, m. 195.5-7.5°, is prepared from Me2CO and the amine. Me 3-amino-5,6,7,8-tetrahydroquinoxaline-2-carboxylate, m. 154-5°, and Me 3-amino-7-chloroquinoxaline-2-carboxylate, m. 224.5-5.5°, are prepared by esterification. Alloxan-H2O (61.44 g.) is treated with 60 g. 3,4-(H2N)2C6H3Cl to give 33% 8-chloroalloxazine, m. 365-6°, and 42% 7-Chloroalloxazine, m. >380°, which is treated at 165° with NH3 in an autoclave to give 68% 3-amino-7-chloroquinoxaline-2-carboxylic acid, m. 191-2° (decomposition). A mixture of 33 g. II (X = NH2, Y = H, Z = Cl), 200 ml. Ac2O, and 200 ml. HC(OEt)3 is refluxed 1.5 hrs. to give 20 g. 4-hydroxy-6-chloropteridine (VI), m. 268-70° (decomposition). VI (5.5 g.) is treated with 4.4 g. PhCH2SH to give 5.5 g. 4-hydroxy-6-benzylthiopteridine (VIII), m. 233-5°. Similarly prepared is 4-hydroxy-6-methylthiopteridine, m. 289.5-91.5°. VII is heated with NaOH to give II (X = OH, Y = H, Z = PhCH2S(VIII), m. 138.9°. Similarly prepared is II (X = OH, Y = H, Z = MeS), m. 182-4° (decomposition). II (X = MeO, Y = Me2N, Z = Cl) (11.5 g.) is treated with 26.3

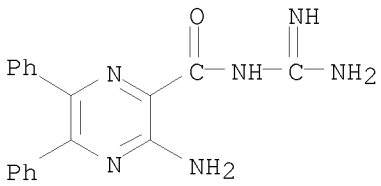
g. H2NC(:NH)NH2.HCl (IX) in the presence of 5.75 g. Na to give 93% (3-amino-5-dimethylamino-6-chloro-2-pyrazinecarbonyl)guanidine (X), m. 216-17°, HCl salt m. 298° (decomposition). Similarly prepared is I.HCl (R = R1 = H, X = Y = Cl) (m. 259-61°) which is treated with Me2NH to give X. II (X = MeO, Y = Me2NCH2CHO, Z = Cl) (9.4 g.) is treated with 20.0 g. IX in the presence of 4 g. Na to give 2.5 g. I.2HCl [R = R1 = H, X = NHC(:NH)NH2, Z = Cl], m. >340°. A solution of 8.5 5. VIII in 50 ml. Ac2O is heated 5 hrs. to give 6.6 g. 2-methyl-6-benzylthio-4H-pyrazine[2,3-d][1,3]oxazin-4-one [IV (X = PhCH2S)] (XI), m. 116.5-18.5°; similarly prepared is IV (X = MeS), m. 189-91°. XI (3.4 g.) is treated with 5.0 g. IX in the presence of 1.0 g. Na to give 1.1 g. I (R = R1 = X = H, Y = PhCH2S), m. 171-3° (decomposition). Also prepared, by the above or related methods, are the following I (R = R1 = H) (X, Y, and m.p. given): NH2, Br, 232.5-5.5° (decomposition); NH2, iodine, 273-4° (decomposition); H, MeS, 203-5°; H, MeSO2, 224-6° (decomposition); OH, H, >310°; NH2, H, 286-8°; Me2N, H, 224-5°; MeO, H, 229-30°; PhCH2NH, H, 231-3°; the following I (R = R1 = H, Y, = Cl) (X and m.p. given): NH2, 240.5-1.5° (HCl salt m. 293.5°); MeNH, 238-9°; EtNH, 217-18°; PrNH, 221-2°; iso-PrNH, 215°; CH2:CHCH2NH, 213-14°; BuNH, 219.5°; sec-BuNH, 208-9°; iso-BuNH, 221°; tert-BuNH, 222-3°; Me(CH2)4NH, 215-16°; BuCHMeNH, 186.5-8.5°; Et2CHNH, 209-11°; Me(CH2)5NH, 194.5-6.5°; cyclopropylmethylamino, 220-1.5°; cyclopropylamino, 213-15°; cyclopentylamino, 219-20°; PhCH2NH, 206-9°; p-MeC6H4CH2NH, 216-17°; o-FC6H4CH2NH, 206-8°; p-ClC6H4CH2NH, 225-6°; PhCH2CH2NH, - (HCl salt m. 199-202°); F3CCH2NH, 232-3°; F3CCH2CH2NH, 221-2.5°; HOCH2CH2NH, - (HCl salt m. 272-3°); HOCH2(CHOH)4CH2NH, 223-4°; H2NCH2CH2NH, - (HCl salt m. 311°); Me2NCH2CH2NH, 192.5-4.5°; 4-pyridylmethylamino, 239-40°; 2-furylmethylamino, 217-18°; PhNH, 246.5-8.5°; p-ClC6H4NH, 276-8°; MeEtN, 229-3°; MeBuN, 214-15°; iso-PrMeN, 207-8°; Me(CH2:CHCH2)N, 207-8°; MeBuN, 208-9°; Et2N, 215°; EtPrN, 224-5°; iso-PrEtN, 207-8°; Et(CH2:CHCH2)N, 208-9°; EtBuN, 200.5-1.5°; Pr2N, 221-2°; PrBuN, 215-17°; 1-pyrrolidinyl, 244.5-5.5°; hexamethylenimino, 224-5°; 4-methylpiperazino, - (2HCl salt m; 229-300°); MeNHNH, 234°; Cl2N, - (HCl salt m. 259-61°); MeNH, 218-19° (decomposition); Me2NNMe, - [2HCl salt m. 262° (decomposition)]; MeNH, 210° (decomposition) [sic]; Me2N, 245° (decomposition); MeBrN, - [HCl salt m. 288° (decomposition)]; EtNH, 207.5-9.5° (decomposition); cyclohexylamino, 221-2° (decomposition); cycloheptylamino, 228-30° (decomposition); cyclopropylamino, 196.5-9° (decomposition); PhNH, 224-6° (decomposition); PhNH, 194.5-5.5° (decomposition)[sic]; Ph2N, 234.5-5.5°; PhClN, 214-16° (decomposition); PhBrN, 234-6° (decomposition); p-ClC6H4NH, 282-5° (decomposition); MePhN, 212-13° (decomposition); MePhN, 218-19° (decomposition)[sic]; Me2NNPh, 204-6° (decomposition); 1-pyrrolidinyl, 220-1°; 1-pyrryl, 211-13°; 3-chloro-1-pyrrolyl, 246-7° (decomposition); (3-isopropylidineamino-6-anilino-2-pyrazinecarbonyl)guanidine, 214-16° (decomposition); (3-acetoamido-6-methylthio-2-pyrazinecarbonyl)guanidine, 220-2°; the following I (X = NH2, Y = Cl) (R, R1, m.p., and m.p. HCl salt given): H, HOCH2CH2, -, 228.5-9.5° (decomposition); H, Ph, -, -, [MeSO3H salt m. 272° (decomposition)]; H, PhCH2, 215-16° (decomposition); -; H, p-FC6H4CH2, 216-19.5° (decomposition), -; H, PhCHMe, 153-60° (decomposition), -; H, 2-C10H7CH2, 243.5-5.5° (decomposition), -; H, 3-pyridylmethyl, 280.5-3.5° (decomposition), -; H, p-MeC6H4CH2, 210-12° (decomposition), -; Me, PhCH2, 274.5° (decomposition), -; H, o-ClC6H4CH2, 220-3° (decomposition), -; H, p-ClC6H4CH2, 204-6° (decomposition), -; H, p-MeOC6H4CH2, 175.5-9.5° (decomposition), -; H,

2,4-Me2C6H3CH2, 220-2° (decomposition), -; H, 2,4-Cl2C6H3CH2, -, 267.5-70.5° (decomposition); H, 3,4-Cl2C6H3CH2, 216-19° (decomposition), -; H, PhClH,CH2, 219-21° (decomposition), -; Me, Me, 240° (decomposition), -, [HCl.H2O salt m. 275° (decomposition)]; H, octahydrol-azocinyl, -, -; Et, Et, 265° (decomposition), -; Bu, Bu, 148-9°, -; (RR1 = ) (CH2)4, -, -; (RR1 = ) 3-oxapentamethylene, -, -; the following I (R = R1 = Me, Y = Cl) (X and m.p. given): iso-PrNH, 238-40.5°; CH2:CHCH2NH, 213-15°; BuNH, 187.5°; cyclopropylmethylamino, 196-7°; Me2N, 219°; MeEtN, 217-18°; iso-PrMeN, 209-11°; Et2N, 212-14°; I (R = H, R1 = HOCH2CH2, X = iso-PrNH, Y = Cl).HCl.0.5H2O [m. 185-6° (decomposition)], and 1-(3,5-diamino-6-chloro-2-pyrazinecarbonyl)2,3-dimethylguanidine.

IT 1634-20-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 1634-20-4 CAPLUS

CN Pyrazinecarboxamide, N-amidino-3-amino-5,6-diphenyl- (7CI, 8CI) (CA INDEX NAME)



L7 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1967:500105 CAPLUS
DOCUMENT NUMBER: 67:100105
ORIGINAL REFERENCE NO.: 67:18835a,18838a
TITLE: Pyrazine diuretics. III. 5- and 6-alkyl, -cyclo-alkyl, and -aryl derivatives of N-amidino-3-aminopyrazinecarboxamides
AUTHOR(S): Bicking, John B.; Robb, Charles M.; Kwong, Sara F.; Cragoe, Edward J., Jr.
CORPORATE SOURCE: Merck and Co. Inc., West Point, PA, USA
SOURCE: Journal of Medicinal Chemistry (1967), 10(4), 598-602
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

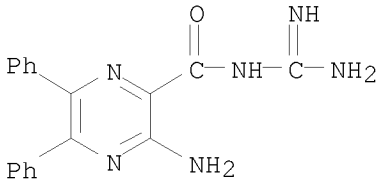
GI For diagram(s), see printed CA Issue.

AB cf. CA 63: 11561e; 66: 37887h. In evaluations of N-amidino-3-aminopyrazinecarboxamides as diuretics, a series of 5- and 6-alkyl, -cycloalkyl, and -aryl derivs. was synthesized and studied for effects on renal electrolyte excretion. Several compds. reverse the electrolyte excretion effects of deoxycorticosterone acetate in the adrenalectomized rat, the most highly active being N-amidino-3-amino-6-methylpyrazinecarboxamide (I). 16 references.

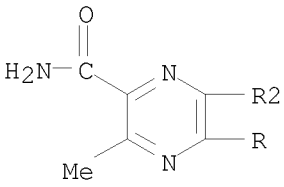
IT 1634-20-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

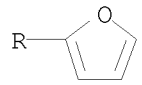
RN 1634-20-4 CAPLUS

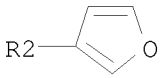
CN Pyrazinecarboxamide, N-amidino-3-amino-5,6-diphenyl- (7CI, 8CI) (CA INDEX NAME)



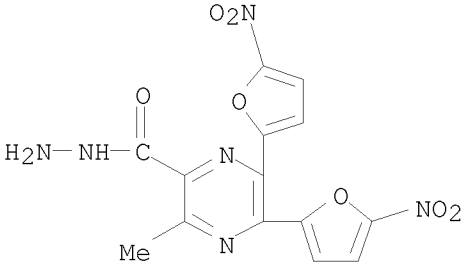
L7 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1967:37882 CAPLUS
DOCUMENT NUMBER: 66:37882
ORIGINAL REFERENCE NO.: 66:7227a,7230a
TITLE: Synthesis of furan derivatives. XXXIV. Preparation of 2,3-bis(5-nitro-2-furyl)pyrazine derivatives
AUTHOR(S): Saikachi, Haruo; Matsuo, Junro
CORPORATE SOURCE: Kyushu Univ., Fukuoka, Japan
SOURCE: Yakugaku Zasshi (1966), 86(10), 927-32
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI For diagram(s), see printed CA Issue.
AB cf. CA 61, 5648a. To a warm (40°) suspension of 19 g. furil in EtOH is added 8 g. ethylenediamine and the whole stirred 2 hrs. to give 20 g. 2,3-di(2-furyl)-5,6-dihydropyrazine (I), m. 128° (dilute EtOH). Similarly prepared is the 5-Me derivative of I, m. 94°, in 70% yield. I (21 g.) is refluxed with 27 g. KCN in 250 ml. 80% EtOH for 30 min., the mixture filtered hot, and 3 vols. H2O is added to the filtrate to give 12 g. 5,6-di(2-furyl)-2-pyrazine-carboxamide (II), yellow plates, m. 182° (EtOH); similarly is prepared the 3-Me derivative, yellow plates, m. 175°. I (21 g.) in 250 ml. 80% EtOH is treated with 4 g. NaOH under introduction of air and 4 vols. H2O added to give 18 g. 2,3-di(2-furyl)pyrazine (III), yellow flakes, m. 81° (EtOH); similarly is prepared the 5-Me derivative, yellow flakes, m. 65°. III (4.2 g.) is dropped into a cold (-10°) mixture of 7.8 g. fuming HNO3 and 18 g. Ac2O, the whole is made to react for 3 hrs., and poured into iced H2O to give 2 g. 2,3-bis(5-nitro-2-furyl)pyrazine, yellow prisms, m. 237° (dioxane); similarly prepared is the 5-Me derivative, yellow plates, m. 197° (AcOH). II (13 g.) is hydrolyzed with 10 g. NaOH in 300 ml. 50% EtOH to give 5,6-di(2-furyl)-2-pyrazine-carboxylic acid (IV), m. 151° (EtOH), almost quant.; the 3-Me derivative, yellow needles, m. 129°. IV (13.5 g.) is esterfied with 300 ml. EtOH and 10 g. concentrated H2SO4 to give 11 g. Et 5,6-di(2-furyl)-2-pyrazinecarboxylate (V), m. 98° (EtOH); the 3-Me derivative, m. 95°. V (2.8 g.) is gradually added to a cold (-5 to -10°) mixture of 3.9 g. fuming HNO3 and 9 g. Ac2O, the whole stirred at the same temperature for 2 hrs., and poured into iced H2O to give 1.2 g. Et 5,6-bis(5-nitro-2-furyl)-2-pyrazinecarboxylate (VI), m. 159° (AcOEt); the 3-Me derivative, yellow plates, m. 134°. VI (1.8 g.) is refluxed in a mixture of 100 ml. 50% AcOH and 2 ml. concentrated H2SO4 for 5 hrs. to give 1.5 g. 5,6-bis(5-nitro-2-furyl)-2-pyrazinecarboxylic acid monohydrate, yellow prisms, m. 197° (EtOH); the 3-Me derivative, yellow needles, m. 206°. (decomposition). Also prepared are the VII tabulated. [TABLE OMITTED]
IT 13480-81-4P 13484-30-5P 13484-31-6P
13484-35-0P 14399-30-5P 15541-91-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 13480-81-4 CAPLUS
CN Pyrazinecarboxamide, 5,6-di-2-furyl-3-methyl- (8CI) (CA INDEX NAME)



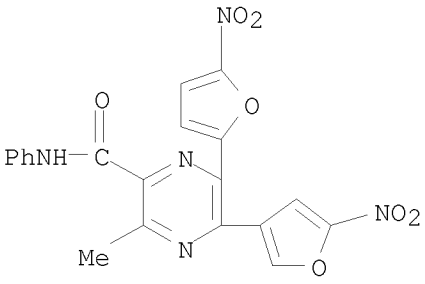




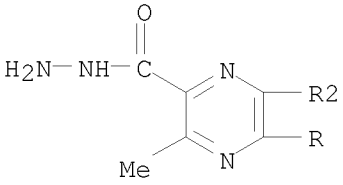
RN 13484-30-5 CAPLUS
CN Pyrazinecarboxylic acid, 3-methyl-5,6-bis(5-nitro-2-furyl)-, hydrazide (8CI) (CA INDEX NAME)

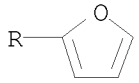


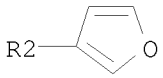
RN 13484-31-6 CAPLUS
CN Pyrazinecarboxanilide, 3-methyl-5,6-bis(5-nitro-2-furyl)- (8CI) (CA INDEX NAME)



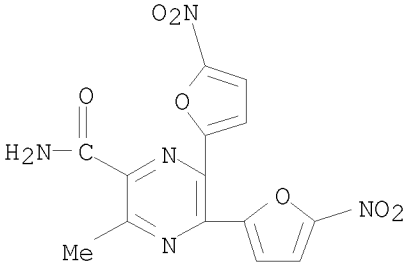
RN 13484-35-0 CAPLUS
CN Pyrazinecarboxylic acid, 5,6-di-2-furyl-3-methyl-, hydrazide (8CI) (CA INDEX NAME)



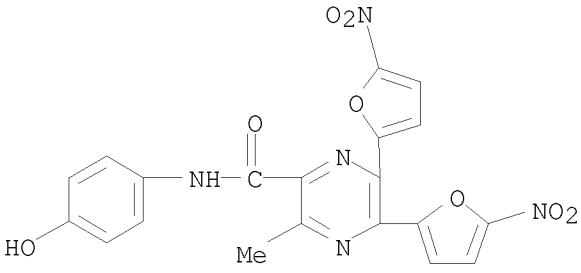




RN 14399-30-5 CAPLUS
CN Pyrazinecarboxamide, 3-methyl-5,6-bis(5-nitro-2-furyl)- (8CI) (CA INDEX NAME)



RN 15541-91-0 CAPLUS
CN Pyrazinecarboxanilide, 4'-hydroxy-3-methyl-5,6-bis(5-nitro-2-furyl)- (8CI) (CA INDEX NAME)



L7 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1965:82636 CAPLUS
DOCUMENT NUMBER: 62:82636
ORIGINAL REFERENCE NO.: 62:14698f-h,14699a-h,14700a-h,14701a-h,14702a-b
TITLE: Substituted guanidines
INVENTOR(S): Cragoe, Edward J., Jr.
PATENT ASSIGNEE(S): Merck & Co., Inc.
SOURCE: 99 pp.

DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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| BE 639386 | | 19640430 | BE | |
| PRIORITY APPLN. INFO.: | | | US | 19621030 |

GI For diagram(s), see printed CA Issue.

AB A suspension of 765 g. Me 3-aminopyrazinecarboxylate in 5 l. C6H6 was treated with 1.99 l. SO2Cl2, refluxed for 5 hrs., and left overnight at room temperature to give 888 g. crude Me 3-amino-5,6-dichloropyrazinecarboxylate (I), m. 233-4°. Into a solution of 100 g. I in 1 l. dry Me2SO dry NH3 was passed under stirring at 65-70° for 45 min., then at 10° for 1.25 hrs. to give 82.5 g. Me 3,5-diamino-6-chloropyrazinecarboxylate (II), m. 212-13°. A mixture of 14.2 g. II, 9 g. Pd-C, 4 g. MgO, and 250 ml. MeOH was shaken under H for 18 hrs. at room temperature to give Me 3,5-diaminopyrazinecarboxylate (III), m. 252-4° (decomposition) (iso-PrOH). Bromination of a suspension of 2 g. III in 25 ml. AcOH at 50° with 2.1 g. Br in 10 ml. AcOH gave 1.2 g. Me 3,5-diamino-6-bromopyrazinecarboxylate (IV), m. 217-19°. Hg(OAc)2 (3.2 g.) and a solution of 2.5 g. iodine in 20 ml. warm dioxane was added rapidly to a suspension of 1.7 g. III in 30 ml. H2O at 70°, the mixture heated for 5 min., cooled to room temperature, and treated with 50 ml. 15% KI solution precipitated 1.2 g. Me 3,5-di-amino-6-iodopyrazinecarboxylate, m. 200-2°. I (11.1 g.), 500 ml. iso-PrOH, 14.4 g. PhNH2, and 12.8 g. PhNH2.HCl was refluxed 24 hrs. under stirring to give 10 g. Me 3-amino-5-anilino-6-chloropyrazinecarboxylate, m. 171.5-73° (iso-PrOH). Similarly were prepared Me 3-amino-5-(p-chloroanilino)-6-chloropyrazinecarboxylate, m. 207-8° (MeCN), and Me 3-amino-5-dimethylamino-6-chloropyrazinecarboxylate (V), m. 145.5-6.5° (MeOH). A solution of 10 g. MeSH in 17 ml. 20% NaOH and 100 ml. MeOH was added to a boiling mixture of 17.7 g. I and 1 l. MeOH and refluxed 15 min. to precipitate 12 g. Me 3-amino-5-methylthio-6-chloropyrazinecarboxylate (VI), m. 212-16° (MeOH). VI (23.4 g.), 35 ml. 30% H2O2, and 300 ml. AcOH was stirred 18 hrs. at room temperature to give 18.5 g. the 5-methylsulfinyl analog (VII), m. 237.5-40.5° (decomposition) (MeOH-AcOEt-HCONH2). Hydrolysis of 7.5 g. VII in 75 ml. AcOH and 12 ml. H2O on a steam bath for 3 hrs. produced 3.7 g. Me 3-amino-5-hydroxy-6-chloropyrazinecarboxylate (VIII), m. .apprx.245° (decomposition) (HCONH2-EtOH). Hydrogenation of VIII with Pd-C and MgO at room temperature resulted in Me 3-amino-5-hydroxypyrazinecarboxylate, decompose 220-60°. Also were prepared Me 3-amino-5-dimethyl-aminopyrazinecarboxylate, m. 242.5-3.5°, Me 3,5-diaminopyrazinecarboxylate, m. 252-4° (decomposition), and Me 3-amino-5-methoxypyrazinecarboxylate, m. 205.5-7.5°. A mixture of 8.9 g. I and 20 ml. PhCH2NH2 was heated on a steam bath for 30 sec. to give 7.5 g. Me 3-amino-5-benzylamino-6-chloropyrazinecarboxylate (IX), m. 157-8° (MeOH). Hydrogenation of IX yielded Me 3-amino-5-benzylaminopyrazinecarboxylate, m. 189.5-91.5°. Treatment of 1.1 g. I with MeONa in 200 ml. boiling absolute MeOH produced 1 g. Me 3-amino-5-methoxy-6-chloropyrazinecarboxylate, m. 255-7° (MeCN). Na2S (9.6 g.) and 10 g. S was refluxed in 80 ml. absolute EtOH. Addition of 8.9 g. I at 25° and stirring for 1 hr. gave 7.8 g. Me 3-amino-5-mercapto-6-chloropyrazinecarboxylate, m. 207-8° (decomposition). To a refluxing solution of 4.44 g. I in 300 mil EtOH was added guanidine (from 1.98 g. guanidine-HCl) in 50 ml. absolute EtOH in 15 min. and

the mixture refluxed 0.5 hr. to give 3.1 g. Me 3-amino-5-ethoxy-6-chloropyrazinecarboxylate, m. 123-5° (iso-PrOH). 3-Amino-6-methylpyrazinoylamide (31 g.) was heated 10 min. with 320 ml. 10% NaOH. The resulting Na salt of the acid (97 g.) was methylated with 77 g. $Me_2SO_4$ in 700 ml. MeOH 19 hrs. at room temperature to give 18 g. Me 3-amino-6-methylpyrazinecarboxylate (X), m. 138.5-40.5° ($C_6H_6$). Chlorination of 9.2 g. X with 65 ml. $SO_2Cl_2$ under cooling produced 4.4 g. Me 3-amino-5-chloro-6-methylpyrazinecarboxylate, m. 108.5-10.5° ($C_6H_6$-cyclohexane). A mixture of 30 g. 3-amino-5-methylpyrazinecarboxylic acid and a solution of 30% HCl in 650 ml. MeOH was stirred 42 hrs. at room temperature to give 15.4 g. Me 3-amino-5-methylpyrazinecarboxylate (XI), m. 165-7° ($H_2O$). A solution of 4.18 g. Br in 3 ml. AcOH was added to a solution of 4.2 g. XI in 15 ml. AcOH in 20 min. to produce 3.6 g. Me 3-amino-5-methyl-6-bromopyrazinecarboxylate, m. 179-81°. Aminomalonamidamidine-2HCl (52.5 g.) was added to an ice-cooled solution of 28.8 g. ethylglyoxal in 450 ml. $H_2O$. The mixture was made alkaline with .apprx.65 ml. concentrated $NH_4OH$ and left 20 hrs. at room temperature to precipitate 17.5 g. 3-amino-6-ethylpyrazinecarboxamide, m. 165.5-8.5° (iso-PrOH), which was saponified 30 min. on a steam bath with 10% NaOH to give 3-amino-6-ethylpyrazine-carboxylic acid (XII), m. 149-52°. Stirring 14 g. XII in a solution of 33% HCl in 160 ml. MeOH 24 hrs. at room temperature gave 4.3 g. XII Me ester, m. 85-7° (iso-PrOH). Also prepared were 3-amino-6-p-chlorophenylpyrazinecarboxylic acid, m. 207-13°, and its Me ester, m. 181.5-3.5°. To a suspension of 17.9 g. 5,6-diaminouracil in 250 ml. $H_2O$ at 60° 14.9 g. cyclohexylgiyoxal-0.5 $H_2O$ was added and the mixture heated 1 hr. on a steam bath to give 7.5 g. 7-cyclohexyllumazine (XIII), m. 229-31° (aqueous AcOH). A solution of 18.5 g. XIII and 9 g. NaOH in 90 ml. $H_2O$ was heated in an autoclave 17 hrs. at 105° to give 8 g. 3-amino-5-cyclohexylpyrazinecarboxylic acid, m. 182.5-3.5° (aqueous iso-PrOH); Me ester m. 173-4.5°. Similarly were prepared Me 3-amino-6-cyclohexylpyrazinecarboxylate, m. 126.5-28°, Me 3-amino-6-cyclopropylpyrazinecarboxylate, m. 112.5-14.5° (amide m. 185.5-7.5°, free acid m. 169-72°), Me 3-amino-5-phenylpyrazinecarboxylate (XIV), m. 231-2°, and Me 3-amino-6-phenylpyrazinecarboxylate (XV), m. 140-1°. Chlorination of 25.6 g. XV with 90 ml. $SO_2Cl_2$ 1.5 hrs. at room temperature gave Me 3-amino 5-chloro-6-phenylpyrazinecarboxylate, m. 187.5-91.5° (AcOH). Bromination of 10.5 g. XIV in 700 ml. AcOH with 11.2 g. Br 21 hrs. at 85° gave 10.5 g. Me 3-amino-5-phenyl-6-bromopyrazinecarboxylate, m. 217-21° (AcOH). To a suspension of 103.59 g. 4,5-diamino-2,6-dihydroxypyrimidine in 1500 ml. $H_2O$ and 500 ml. concentrated $NH_4OH$ at 60° 103.71 g. 1-phenyl-1,2-propanedione was added and the mixture heated at 90° under vigorous stirring to give 82.4 g. 6(or 7)-methyl-7(or 6)-phenyllumazine, m. 281.5-2.5° (AcOH), and 32 g. 6(or 7)-phenyl-7(or 6)-methyllumazine (XVI), m. 254.5-5.5°. Saponification of XVI with 8% NaOH in an autoclave 3.5 hrs. at 170° gave 3-amino-5(or 6)-phenyl-6(or 5)-methylpyrazinecarboxylic acid, m. 193.5-4.5°; Me ester m. 163-4° (MeOH). Similarly were prepared 3-amino-5(or 6)-methyl-6(or 5)-phenylpyrazine carboxylic acid, m. 155-6°; Me ester m. 162.5-3.5° (MeOH). Me 3-amino-6-phenylpyrazinecarboxylate was chlorinated with $SO_2Cl_2$ to give Me 3-amino-5-chloro-6-phenylpyrazinecarboxylate, m. 187.5-90.5° (AcOH), and subsequently treated with $Me_2NH$ in MeOH to give Me 3-amino-5-dimethylamino-6-phenylpyrazinecarboxylate, m. 167.5-9.5° (MeOH). To 750 ml. AcOH and 3180 ml. $H_2O$ at 38°, 90 g. Me 3-aminopyrazinecarboxylate was added and Cl passed through in 25 min. to give Me 3-amino-6-chloropyrazinecarboxylate (XVII) m. 142° (decomposition) ($H_2O$). A solution of 18.8 g. XVII, 15 g. $PhNH_2$, and 2.5 ml. concentrated HCl in 150 ml. $Me_2CO$ was refluxed 16 hrs. to give 7.4 g. Me 3-isopropylideneamino-6-anilinopyrazinecarboxylate, m. 195.5-7.5° (iso-PrOH). A mixture of

9.3 g. 3-amino-5,6,7,8-tetrahydroquinoxaline-2-carboxylic acid and 230 ml. absolute MeOH of 10° was treated with 30 ml. concentrated $H_2SO_4$ in 1 hr. and left 24 hrs. at room temperature to give 1.6 g. the Me ester, m. 154-5° (1:5 MeOH-$H_2O$). A solution of 60 g. 4-chloro-o-phenylenediamine in 60 ml. $H_2O$ and 50 ml. 12N HCl was treated with a solution of 61.44 g. alloxan-$H_2O$ in 100 ml. $H_2O$ and stirred 1 hr. at 90° to give a precipitate of 78.4 g. 8-chloroalloxazine, m. 365-6° and 40.36 g. 7-chloro-alloxazine, (XVIII) m. 380° ($Me_2SO$). A mixture of 44.2 g. XVIII and 190 ml. concentrated $NH_4OH$ was heated in an autoclave 10 hrs. at 165° to give 27.2% 3 amino-7-chloroquinoxalin-2-carboxylic acid, m. 191-2° (decomposition); Me ester m. 224.5-5.5° (MeCN). Also prepared are the following XIX (R, R1, % yield, and m.p. given): Me, H, 88, 221-2°; Et, H, 89, 149-50°; Pr, H, 75, 138-40°; iso-Pr, H, 70, 125.5-6.5°; $CH_2$:$CHCH_2$, H, 69, 105-6.5°; Bu, H, 91, 140-2°; sec-Bu, H, 75, 106-8°; iso-Bu, H, 51, 113.5-15.5°; tert-Bu, H, 38, 98-108°; Am, H, 72, 100.5-2.5°; MePrCH, H, --, --; $Et_2CH$, H, --, --; $C_6H_{13}$, H, 70, 72.5-5.5°; cyclopropylnethyl, H, 78, 132-3° cyclopropyl, H, 98, 167-9°; cyclopentyl, H, 93, 119.5-21.5°; $PhCH_2$, H, 64, 157-8°; p-$MeC_6H_4CH_2$, H, 66, 112.5-14.5°; o-$FC_6H_4CH_2$, H, 84, 171-4°; p-$ClC_6H_4CH_2$, H, 93, 136-7°; $PhCH_2CH_2$, H, 59, 115-19°; $CF_3CH_2$, H, 97, 153-4° $CF_3CH_2CH_2$, H, 76, 124.5-5.5°; $HOCH_2CH_2$, H, 100, 155-7°; $HOCH_2(CHOH)_4CH_2$, H, 60, 172-5°; $NH_2CH_2CH_2$, H, 96, 265°; $Me_2NCH_2CH_2$, H, 40, 257°; 4-pyridylmethyl, H, 69, 95-7°; 2-furylmethyl, H, 81, 148-9°; Me, Et, 73, 102-4°; Me, Pr, 58, 83.5-5.5°; Me, iso-Pr, 78, 75.5-7.5°; Me, $CH_2$:$CHCH_2$, 70, 90.5-92°; Me, Bu, 74, 59.5-61.5°; Et, Et, 54, 99-101°; Et, Pr, --, --; Et, iso-Pr, --, --; Et, $CH_2$:$CHCH_2$, --, --; Et, Bu, 91, 77.5-9.5°; Pr, Bu,--, --; Pr, Pr, 66, 68.5-71.5°; (NRR1 = ) pyrrolidino, 95, 168-71°; (NRR1 =) 1 (hexahydroazepinyl), 75, 109-11°; (NRR1 =) N'-Methylpiperazino, 88, 186-8°; Me, $NH_2$, 67, 136.5-38°

Guanidine-HCl (XX) (26.3 g.) was added to a solution of MeONa (5.75 g. Na in 150 ml. absolute MeOH), the precipitated NaCl filtered off, and the filtrate concentrated to 30 ml. After addition of 11.5 g. V the mixture was boiled 1 min., then maintained 1 hr. at room temperature to give 93% (3-amino-5-dimethylamino-6-chloropyrazinecarbonyl) guanidine (XXa), m. 216-17°; HCl salt m. 298° (decomposition). Similarly were prepared (3,5-diamino-6-bromopyrazin-carbonyl)guanidine, m. 232.5-5.5° (decomposition), (3,5-diamino-6-iodopyrazinecarbonyl)guanidine-HCl, m. 273-4° (decomposition) and (3-isopropylideneamino-6-anilinopyrazinecarbonyl)guanidine, m. 214-16° (decomposition). To a solution of 920 mg. Na in 50 ml. absolute iso-PrOH 3.85 g. XX was added and the NaCl filtered off. Adding 4.4 g. I and refluxing the mixture 15 min. gave (3-amino-5,6-dichloropyrazinecarbonyl)guanidine HCl salt (XXb) m. 259-61°. The solution of XXb in 5 ml. HCONMe2 was treated with 1 ml. 25% aqueous $Me_2NH$ 1 hr. on a steam bath to give XXa. Reaction of 11.1 g. I with 55 ml. $Me_2NCH_2CH_2OH$ 20 min. on a steam bath gave 9.5 g. Me 3-amino-5-(2-dimethylamino-ethoxy)-6-chloropyrazinecarboxylate (XXI), m. 134.5-6.5° (C6H6-cyclohexane). To 20 g. XX in iso-PrONa (4 g. Na in 100 ml. iso-PrOH) 9.4 g. XXI was added and the mixture heated 30 min. on a steam bath to give 2.5 g. (3-amino-5-guanidino-6-chloropyrazinecarbonyl)guanidine-2HCl, m. >340°. A mixture of 2 1. concentrated $NH_4OH$ and 300 g. XVIII was stirred 16 hrs. at room temperature to give 260 g. 3-amino-6-chloropyrazinecarboxamide (XXII), m. 227-30°. $HC(OEt)_3$ (200 ml.) and 33 g. XXII refluxed in 200 ml. $Ac_2O$ 1.5 hrs. gave 20 g. 4-hydroxy-6-chloropteridine (XXIII), m. 268-70° (decomposition) (iso-PrOH). A solution of 5.5 g. XXIII and 4.4 g. $PhCH_2SH$ in 100 ml. 4% NaOH was heated 30 min. on a steam bath to give 5.5 g. 4-hydroxy-6-benzylthiopteridine, m. 233-5° (aqueous iso-PrOH), which was converted

into 3-amino-6-benzylthiopyrazinecarboxylic acid (XXIV), m. 138-9°, by 8 hrs. hydrolysis with 5% NaOH. XXIV (8.5 g.) in 50 ml. Ac2O was heated 5 hrs. on a steam bath to give 6.6 g. 2-methyl-6-benzylthio-4H-pyrazino[2,3-d][1,3]oxazin-4-one (XXV), m. 116.5-18.5° (C6H6). To 1 g. Na in 30 ml. iso-PrOH 5 g. XX and 3.4 g. XXV were added to give, after 1 hr. at room temperature, 1.1 g. (3-amino-6-benzylthiopyrazinecarbonyl-guanidine, m. 171-3° (decomposition). Similarly were prepared 4-hydroxy-6-methylthiopteridine, m. 289.5-91.5° (aqueous iso-PrOH), 3-amino-6-methylthiopyrazinecarboxylic acid (XXVI), m. 182-4° (decomposition) (AcOEt), 2-methyl-6-methylthio-4H-pyrazino[2,3-d][1,3]oxazin-4-one, m. 189-91° (C6H6), and 3-acetamido-6-methylthiopyrazinecarbonyl)guanidine (XXVII), m. 220-2°. Addition of HCl to XXVII in H2O gave 86% (3-amino-6-methyl-thiopyrazinecarbonyl)guanidine, m. 203-5°. A solution of 0.92 g. XXVI in 15 ml. 2.5% NaOH was treated with 1.05 g. KMnO4 in 35 ml. H2O to give 0.5 g. 3-amino-6-methylsulfonylpyrazine-carboxylic acid, m. 239-42° (decomposition) (iso-PrOH), which gave, after 5 hrs. heating in Ac2O, 2-methyl-6-methylsulfonyl-4H-pyrazino[2,3-d][1,3]oxazin4-one, m. 214-16° (Me2CO), transformed into 27% 3-amino-6-methylsulfonylpyrazinecarbonyl)guanidine, m. 224-6° (decomposition) (iso-PrOH). Similarly are prepared the following XXVIIa (R, R1, % yield, and m.p. given): H, H, 93, 240.5-1.5°; 293.5° (HCl salt); Me, H, 89, 238-9°; Et, H, 63, 217-18°; Pr, H, 93,221-2°; iso-Pr, H, 75, 215°; CH2:CHCH2, H, 84, 213-14°; Bu, H, 65, 219.5°; Me-ETCH, H, 74, 208-9°; iso-Bu, H, 76, 221°; tert-Bu, H, 84, 222-3°; Am, H, 70, 215-16°; MePrCH, H, 89, 186.5-8.5°; Et2CH, H, 82, 209-11°; C6H13, H, 100, 194.5-6.5°; cyclopropylmethyl, H, 95, 220-1°; cyclopropyl, H, 85, 213-15°; cyclopentyl, H 65, 219-20°; PhCH2, H, 44, 206-9°; p-MeC6H4CH2, H, 57, 216-17°; o-FC6H4CH2, H, 100, 206-8°;. p-ClC6H4CH2, H, 96, 225-6°; PhCH2CH2, H, 57, 199-202°; CF3CH2, H, 77, 232-3°; CF3CH2CH2, H, 65, 221-2.5°; HO-CH2CH2, H, 63, 272-3°; HOCH2(CHOH)4CH2, H, 68, 223-4°; NH2CH2CH2, H, 68, 311°; Me2NCH2CH2, H, 98, 192.4-4.5°; 4-pyridylmethyl, H, 64, 239-40°; o-furylmethyl, H, 92, 217-18°; Ph, H, 95, 246.5-8.5°; p-ClC6H4, H, 95, 276-8°; Me, Et, 92, 229-30°; Me, Pr, 97, 214-15°; Me, iso-Pr, 70, 207-8°; Me, CH2:CHCH2, 95, 207-8°; Me, Bu, 95, 208-9°; Et, Et, 75, 215°; Et, Pr, 92, 224-5°; Et, iso-Pr, 75, 207-8°; Et, CH2:CHCH2, 92, 208-9°; Et, Bu, 98, 200.5-1.5°; Pr, Pr, 100, 221-2°; Pr, Bu, 84, 215-17°; (NRR1 =) pyrrolidino, 90, 244.5-5.5°; (NRR1 =) 1-hexahydroazepinyl, 49, 224-5°; (NRR1 =) N-methylpiperazino, 74, 299-300°; Me, NH2, 92, 234°.
Also prepared are the following XXVIIb (X, Y, % yield, and m.p. base and m.p. HCl salt given): H, HO, 10, >310° (decomposition); H, NH2, 8, 286-8° (decomposition), --; H, NMe2, 45, 224-5° (decomposition), --; H, MeO, 52, --, 229-30° (decomposition); H, PhCH2NH, 56, --, 231-7° (decomposition); Cl, MeO, 90, --, 257°; Cl, MeS, 100, 234.5-6.5°, --; Cl, HO, 24, --, >300° (decomposition); Cl, SH, 100, 236.5° --; Cl, EtO, 81, 215-16° --; Cl, Cl, 72, --, 259-61°; Me, H, 87, 218-19 (decomposition), --; Me, Me2N, 42, --, 262° (decomposition) (di-HCl); H, Me, 13,210° (decomposition), --; Me, Me, 38, 245° (decomposition), --; Br, Me, 35, 288° (decomposition), --; Et, H, 53, 207.5-9.5° (decomposition), --; H, cyclohexyl, 71, 221-2° (decomposition), --; cycloheptyl, H, 61, 228-30° (decomposition), --; cyclopropyl, H, 61, 196.5-99° (decomposition), --; H, Ph, 51, 224-6° (decomposition); Ph, H, 34, 194.5-5.5° (decomposition), --; Ph, Ph, 87, 234.5-5.5°, -; Ph, Cl, 69, 214-16° (decomposition), --; Br, Ph, 66, 234-6° (decomposition), --; p-ClC6H4, H, 70, 282-5° (decomposition), --; Me (or Ph), Ph (or Me), 77, 212-13° (decomposition), --; Ph (or Me), Me (or Ph) 90, 218-19° (decomposition), --;

Ph, Me2N, 40, 205-6° (decomposition), --; (XY =)(CH2)4, 29, 220-1°, --; (XY =) CH:CHCH:CH, 56, 211-13°, --; (XY =) HC:CClCH:CH, 70, 246-7° (decomposition), --. A solution of 13.9 g. 2-methyl-2-pseudothiuronium sulfate (XXVIII) and 9.2 g. H2NCH2CH2OH in 40 ml. H2O was heated 20 min. to give 12.5 g. (2-hydroxyethyl)guanidine sulfate, m. 127.5-35.5°, which was added to a solution of 2g. Na in 25 ml. MeOH, MeOH distilled, and the residue treated with 4.1 g. II 5 min. on steam bath to give 1.2 g. 1-(3,5-diamino-6-chloropyrazinoyl)-3-(2-hydroxyethyl)guanidine-HCl, m. 228.5-9.5° (aqueous iso-PrOH). 1-(3-Amino-5-isopropylamino-6-chloropyrazinoyl)-3-(2-hydroxyethyl)guanidine-HCl.0.5H2O, m. 185-6° (decomposition), was prepared from Me 3-amino-5-isopropylamino-6-chloropyrazinecarboxylate. A mixture of 6.1 g. II, 6.8 g. phenylguanidine, and 3 ml. iso-PrOH was heated 6 hrs. to give 1-(3.5-diamino-6-chloropyrazinoyl)-3-phenylguanidine, isolated as the MeSO3H salt, m. 272° (decomposition) (H2O). Ph-CH2NH2 (80.3 g.) and 69.5 g. XXVIII in 200 ml. H2O kept 18 hrs. at room temperature gave benzylguanidine sulfate, which was converted into the HCl salt (XXIX) (51.5 g.), m. 175-8° (aqueous EtOH), by treating its aqueous solution with aqueous BaCl2. To a solution of 1 g. Na in 30 ml. iso-PrOH 9.3 g. XXIX was added and half the volume distilled Addition of 2 g. II and heating the mixture 15 min. yielded 1 g. 1-(3,5-diamino-6-chloropyrazinoyl)-3-benzylguanidine, m. 215-16° (decomposition) (aqueous iso-PrOH). With the appropriate starting materials the following 3-substituted 1-(3,5-diamino-6-chloropyrazinoyl)guanidines were prepared [3-substituent and m.p. (decomposition) given]: p-fluorobenzyl 216-19.5°; α-methylbenzyl 153-60°; 3-pyridylmethyl, 280.5-3.5°; 2-naphthylmethyl 243.5-5.5°. Also prepared were the following RR1-NC(:NH)NH2.HCl (R, R1, % yield, and m.p. given): p-Me-C6H4CH2 H, 28, 153-5°; o-ClC6H4CH2, Me, 32, 122.5-5.5°; PhCH2, H, 71, 131-6°; p-ClC6H4CH2, H, 55, 162.5-4.5°; p-MeOC6H4CH2, H, 69, 132-7°; 2,4-Me2C6H3CH2, H, 52, 105-15°; 2,4-Cl2C6H3CH2, H, 67, 145-8°; 3,4-Cl2C6H4CH2, H, 77, 155-7°; PhCH2CH2, H, 71, 135-8°.

Also prepared were the following XXIXa [R, R1, % yield, and m.p. (decomposition)given]: p-MeC6H4CH2, H, 27, 210-12°; PhCH2, Me, 35, 274.5° (HCl salt); o-ClC6H4CH2, H, 39, 220-3°; p-ClC6H4CH2, H, 46, 204-6° p-MeOC6H4CH2, H, 27, 175.5-9.5°; 2,4-Me2C6H3CH2 H, 59, 220-2°; 2,4-Cl2C6H3CH2, H, 30, 267.5-70.5° (HCl salt); 3,4-Cl2C6H3CH2, H, 47, 216-19°; PhCH2CH2, H, 46, 219-21.5°. To a solution of 2.3 g. Na in 200 ml. absolute MeOH 15 g. dimethyl-guanidine sulfate was added, the mixture refluxed 1 hr. and cooled, Na2SO4 filtered off, the solution concd, to 30 ml., 10.15 g. II added, and the mixture heated 30 min. and kept 1 hr. at room temperature to give 3.6 g. 1-(3,5-diamino-6-chloropyrazinoyl)-3,3-dimethyl-guanidine (XXX), decomposing at 240° HCl salt m. 275° (decomposition). To a solution of 36.57 g. Et2NH in 100 ml. H2O and 41 ml. concentrated HCl adjusted, with 3.66 g. Et2NH to pH 9.2 a solution of 50% aqueous cyanamide (65.16 g.) was added dropwise at 100° in 4 hrs. After refluxing 1 hr. and standing over night at room temperature the mixture was treated with 50 ml. of 40% NaOH and CO2 passed through under cooling to give 1,1-diethylguanidine, isolated as the HCl salt (XXXI) (35 g.), m. 147-9°. Similarly, 1,1-dibutylguanidine-HCl (XXXII), m. 104.5-106° (H2O), was obtained in 86% yield. The following compds. were also prepared: 88.6% 1 - (3,5-diamino-6-chloropyrazinoyl)-3,3-diethylguanidine, m. 265° (decomposition), from II and XXXI and 72% 1-(3,5-diamino-6-chloropyrazinoyl)-3,3-dibutylguanidine, m. 148-9° (iso-PrOH), from II and XXXII.

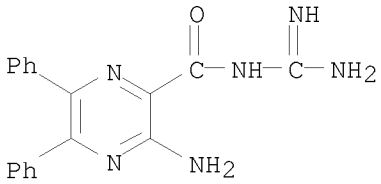
Also prepared were the following XXXIII (R, R1, % yield, and m.p. given): iso-Pr, H, 35, 238.5-40°; CH2:CHCH2, H, 39, 215°; Bu, H, 17,

187.5°; cyclopropylmethyl, H, 3, 196-7°; Me, Me, 69, 219°; Me, Et, 49, 218°; Me, iso-Pr, 61, 209-11°; Et, Et, 40,214°. The compds. are effective in the treatment of abnormal electrolyte excretion.

IT 1634-20-4P, Pyrazinecarboxamide, N-amidino-3-amino-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)

RN 1634-20-4 CAPLUS

CN Pyrazinecarboxamide, N-amidino-3-amino-5,6-diphenyl- (7CI, 8CI) (CA INDEX NAME)



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TITLE: Pteridines. XXIII. A facile pyrimidine ring cleavage

AUTHOR(S): Taylor, Edward C., Jr.; Knopf, Robert J.; Cogliano, J. A.; Barton, J. W.; Pfleiderer, Wolfgang

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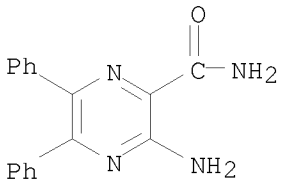
AB cf. CA 55, 551g. 4-Mercaptopteridines and -pyrimidines were readily cleaved by ClCH2CO2H (I) and alkali carbonate or MeI and alkali. The results of a study of this cleavage indicated that heterocyclic systems containing a fused 4-substituted pyrimidine ring underwent a base-catalyzed cleavage to an o-aminonitrile, provided that the anion formed by attack of base at C-2 of the fused pyrimidine ring was capable of stabilization by appropriate structural features in the remainder of the mol., and that the substituent group attached to C-4 was capable of departure with its bonding pair of electrons in an irreversible cleavage step. These results underscored a fundamental chemical difference between purines and pteridines. 4-Mercapto-6,7-diphenylpteridine (0.2 g.) and 0.1 g. I in 15 cc. N NaHCO3 refluxed 0.5 hr. and filtered hot gave 0.12 g. 2-amino-3-cyano-5,6-diphenylpyrazine (II), m. 160-3°; the aqueous phase from a similar run with a slight deficiency of Na2CO3 treated with AgNO3 gave the insol. Ag salt of HSCH2CO2H. II (0.54 g.), 0.16 g. NaOH, and 2 cc. 30% H2O2 in 25 cc. 40% aqueous EtOH refluxed 3 hrs. gave 0.40 g. 2-amino-5,6-diphenylpyrazine-3-carboxamide (III), yellow needles, m. 202-5°. II (1.4 g.) in 100 cc. 95% EtOH containing a few drops N(CH2CH2OH)3 treated 3 hrs. at 50-5° with H2S, the whole cooled, and filtered yielded 1.3 g. 3-CSNH2 analog of III, yellow needles, m. 158-60°. 4-Mercaptopteridine (IV) (0.5 g.), 0.45 g. I, 0.81 g. Na2CO3, and 30 cc. H2O refluxed 6 min., the mixture cooled to 0°, and filtered after 12 hrs. at 0° yielded 0.12 g. 2-amino-3-cyanopyrazine (V), needles, m. 192°; 0.04 g. 2nd crop. 4-MeS analog (VI) (0.54 g.) of V and 20 cc. N NaHCO3 refluxed 6 min., the mixture filtered, and the filtrate evaporated,

the residue sublimed at 150°/0.5 mm., and the sublimate (0.2 g.) extracted with Et2O left 0.07 g. 2-aminopyrazine-3-carboxamide (VII), needles, m. 235°; the residue from the Et2O extract recrystd. from H2O gave 0.09 g. V, needles, m. 188-90°; the sublimation residue recrystd. from H2O gave a small amount of 4-hydroxypteridine (VIII). VI (0.18 g.) and 10 cc. N NaHCO3 refluxed 2 min., the mixture filtered hot, and the filtrate cooled gave 0.1 g. unchanged VI, m. 194°; the filtrate contained V, VII, and VIII. VI (0.16 g.) and 10 cc. N NaHCO3 refluxed 45 min. gave a mixture of VI, VIII, and 2-amino-3-carboxylic acid; the mixture evaporated, and the residue sublimed at 150°/0.5 mm. yielded 0.07 g. VII, m. 230°. VI (0.16 g.) and 10 cc. N AcOH refluxed 1 hr. (MeSH evolved), the solution filtered hot with C, and cooled to 0° yielded 0.1 g. VIII. HC(OEt)3 (60 cc.), 60 cc. Ac2O, and 8.0 g. 4-aminopyridine-5-carboxamide refluxed 3 hrs., the solution concentrated to about 1/3 of the original volume, diluted with 150 cc. dry Et2O, and cooled to 0° gave 6.30 g. 4-hydroxypyrimido[4,5-d]pyrimidine (IX), needles, m. 253-5° (decomposition) (H2O). Powdered IX (3.70 g.) and 5.55 g. P2S5 in 20 cc. dry C5H5N refluxed 45 min., the mixture kept 15 min., poured with stirring into 50 cc. H2O and 50 g. crushed ice, stirred 0.5 hr., kept 12 hrs. at 0°, and filtered gave 3.80 g. 4-SH analog (X) of IX, bright yellow, did not melt but darkened rapidly above 300° (sublimed at 230°/0.1 mm.). X (0.66 g.) in 16 cc. 1% aqueous NaOH treated at 0-5° with 0.20 cc. MeI, the mixture stirred 1.5 hrs., filtered, and refrigerated overnight gave 0.40 g. 4-MeS analog (XI) of IX, m. 159-60° (sublimed at 130°/0.05 mm.). X (0.70 g.), 0.75 g. NaOH, and 12 cc. H2O stirred at room temperature to solution and then 2 hrs. with 1.0 g. MeI, the whole cooled, and filtered gave 0.25 g. 4-amino-5-cyanopyrimidine, needles, m. 250-2° (H2O); also obtained in 82% yield by stirring XI in dilute aqueous NaOH at room temperature 4-Hydroxypyrido[3,4-d]pyrimidine (10 g.) and 59 g. P2S5 in 250 cc. dry C5H5N refluxed 2 hrs. and the solution evaporated in vacuo, the residue treated with 500 cc. H2O, the mixture refluxed 20 min. after 12 hrs., and filtered, and the filter residue dissolved in 15 cc. H2O and 20 cc. concentrated NH4OH, the solution filtered, and added dropwise to 300 cc. refluxing H2O and 50 cc. AcOH gave 9.0 g. 4-mercaptopyrido[3,4-d]pyrimidine (XII) derivative of X, m. 325° (decomposition). XII (2.0 g.) in 20 cc. N NaOH and 10 cc. H2O shaken 5 min. with 1.5 cc. Me2SO4 and filtered gave 1.5 g. 4-MeS analog of XII. 4-Aminonicotinic acid (XIII) (36 g.), 500 cc. absolute EtOH, and 36 cc. concentrated H2SO4 refluxed 70 hrs. on the steam bath and the whole worked up gave 31 g. Et ester (XIV) of XIII, m. 100-5°. XIV (25 g.) and 50 cc. HCONH2 heated 1 hr. at 160°, the mixture refluxed 3 hrs., cooled, and filtered yielded 10 g. 4-hydroxypyrido[4,3-d]pyrimidine (XV), m. 293° (H2O); 3.5 g. 2nd crop. XV was converted in the usual manner to the 4-SH analog (XVI) of XV, yellow, m. 323-5° (decomposition) (EtOH). XVI (1 g.), 0.9 g. I, 1.8 g. Na2CO3, and 30 cc. H2O refluxed 20 min., the mixture filtered, and cooled gave 0.15 g. 2-aminonicotinonitrile (XVII), m. 131°; the filtrate evaporated, and the residue sublimed at 120°/0.5 mm. gave 0.05 g. XVII; further sublimation at 200° yielded 0.1 g. 2-aminonicotinamide, m. 199°. XII (1 g.), 0.9 g. I, 1.8 g. Na2CO3, and 30 cc. H2O refluxed 20 min., the mixture filtered, and acidified to pH 2 with dilute HCl gave 0.7 g. 4-HO2CCH2S analog of XII, needles, m. 221° (decomposition); the filtrate chilled 4 days yielded 0.12 g. [3,4-d]-isomer (XVIII) of XV, m. 305°. XVI (1 g.), 0.9 g. I, 1.8 g. Na2CO3, and 30 cc. H2O refluxed 20 min. and worked up gave 0.45 g. 4-isomer of XVII, m. 173°. 9-Methyl-6-mercaptopurine (1.0 g.) in 10 cc. H2O containing 0.9 g. I and 1.8 g. Na2CO3 refluxed 35 min., the mixture cooled to room temperature, and acidified with dilute HCl gave 1.25 g.

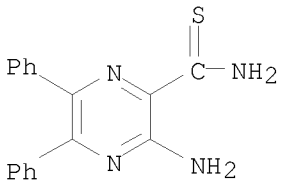
9-methyl-6-carboxymethylthiopurine, m. 225-6° (hot 30% aqueous EtOH). 6-Nitro-4-quinazolone (1.0 g.), 1.5 g. P2S5, and 15 cc. dry C5H5N refluxed 0.5 hr., the whole cooled, poured onto crushed ice, filtered after 2 hrs., and the residue repptd. with AcOH from dilute aqueous NaOH gave 0.93 g. 4-mercapto-6-nitroquinazoline (XIX), bright yellow needles, m. 261-3° (decomposition) (aqueous C5H5N). The 7-NO2 and the 8-NO2 isomers (XX) of XIX, bright yellow needles, m. 270-1° (decomposition) (aqueous C5H5N), and yellow needles, m. 266-7° (decomposition) (aqueous C5H5N), resp., were prepared in 67 and 46%, resp., yields from 7- and 8-nitro-4-quinazolone, resp. 5-Nitro-4-quinazolone (6 g.) and 10.5 g. PCl5 heated 3 hrs. at 150°, the mixture cooled, diluted with 150 cc. petr. ether (b. 60-70°), cooled 1 hr. at 0°, and filtered, the residue stirred 10 min. with dilute aqueous NaOH, ice, and CH2Cl2, and the organic layer worked up yielded 4.7 g. 4-chloro-5-nitroquinazoline (XXI), needles, m. 146-7° (sublimed at 130°/0.1 mm.). XXI (1 g.) in 20 cc. dioxane treated with stirring at room temperature with KSH (from 0.3 g. KOH) in 20 cc. absolute EtOH, the whole diluted after 1 hr. with 20 cc. Et2O, and filtered, and the residue added rapidly with stirring to 10 cc. H2O, 0.25 g. NaOH, and 0.4 cc. MeI, and the mixture filtered after 20 min. yielded 0.55 g. 4-methylthio-5-nitroquinazoline, pale yellow flakes, m. 146-7° (petr. ether). XIX (7.35 g.), 400 cc. H2O, 6.8 g. KOH, and 8.4 g. MeI stirred 4 hrs. at room temperature gave 7.2 g. 4-MeS analog (XXII) of XIX, m. 162-3°(absolute EtOH). XIX (1 g.), 0.5 g. I, and 20 cc. H2O refluxed 0.5 hr., the mixture cooled to 0°, and filtered gave 0.43 g. 5-nitroanthranilonitrile (XXIII), m. 210-11° (sublimed at 140°/0.05 mm.). XXII (0.5 g.), 1.24 g. KOH, 40 cc. H2O, and 60 cc. dioxane stirred 2 hrs. at room temperature, the solution concentrated, and cooled yielded 0.032 g. XXIII, m. 210°. XX (1 g.) treated with I and K2CO3 in the usual manner gave 0.085 g. 3-isomer of XXIII, yellow needles, m. 137-8° (sublimed at 100°/0.01 mm.).

IT 101445-25-4P, Pyrazinamide, 3-amino-5,6-diphenyl-
110490-39-6P, Pyrazinamide, 3-amino-5,6-diphenylthio-
RL: PREP (Preparation)
(preparation of)

RN 101445-25-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)




RN 110490-39-6 CAPLUS
CN Pyrazinamide, 3-amino-5,6-diphenylthio- (6CI) (CA INDEX NAME)



L7 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1958:55949 CAPLUS
DOCUMENT NUMBER: 52:55949
ORIGINAL REFERENCE NO.: 52:10106g-i,10107a-i,10108a-i
TITLE: Pteridines. XVI. A synthesis of 2-aminopyrazine-3-carboxamides by reductive ring cleavage of 3-hydroxy-1-pyrazolo[b]pyrazines
AUTHOR(S): Taylor, E. C., Jr.; Barton, J. W.; Osdene, T. S.
CORPORATE SOURCE: Princeton Univ., Princeton, NJ
SOURCE: Journal of the American Chemical Society (1958), 80, 421-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 52:55949

AB cf. C.A. 50, 13047b. PhN:NCH(CN)CO2Et (I) (4.1 g.) and 25 cc. EtOH refluxed 15 min. with 1.4 g. N2H4.H2O, cooled to 0°, and filtered yielded 3.6 g. 3-hydroxy-4-phenylazo-5-aminopyrazole (II), deep red needles, m. 256° (decomposition). HON:C(CN)CONHNH2 N2H4 salt (III) (5.0 g.) in 25 cc. 40% aqueous NaOH kept 1 hr. at 60°, acidified with glacial AcOH, and filtered gave 3.87 g. 3-hydroxy-4-nitroso-5-aminopyrazole (IV); a similar run heated 0.5 hr. on the steam bath gave 2.56 g. IV. III (5.0 g.) in 100 cc. EtOH containing 6 g. Na refluxed 4 hrs. with stirring and filtered, and the residue dissolved in 25 cc. H2O, acidified with glacial AcOH, and cooled gave 4.0 g. IV. II (4.0 g.) in 50 cc. 98% HCO2H hydrogenated at 3 atmospheric over 0.4 g. 10% Pd-C, filtered, and evaporated, the residue triturated with 1:1 EtOH-Et2O, and the undissolved material recrystd. with C from H2O gave 2.95 g. diformyl derivative (V) of 3-hydroxy-4,5-diaminopyrazole (VI), m. 212-13° (decomposition). IV (2.0 g.) in 40 cc. 98% HCO2H hydrogenated over 10% Pd-C yielded 2.05 g. V. V (8 g.) in 30 cc. 50% H2SO4 warmed to beginning crystallization, diluted with boiling H2O to solution, and cooled slowly yielded 9.4 g. VI.H2SO4, light yellow crystals. I (32.5 g.), 7.5 cc. 99% MeNHNH2, and 250 cc. EtOH refluxed 4 hrs. and cooled to 0° gave 27 g. 1-Me derivative (VII) of II, m. 265° (EtOH). HON:C(CN)CO2Et (7.1 g.), 5 cc. 99% MeNHNH2, and 30 cc. EtOH refluxed 3 hrs., refluxed 1 hr. with stirring with 30 cc. 30% alc. KOH, cooled to 0°, and filtered, and the residue dissolved in 20 cc. H2O and adjusted with AcOH to pH 5 yielded 2.9 g. 1-Me derivative (VIII) of IV, m. 184-6°; 2nd crop, 0.3 g. VII (20 g.) in 100 cc. 90% HCO2H hydrogenated 45 min. at 3 atmospheric over 1 g. 10% Pd-C, filtered, and evaporated in vacuo, the residual oil washed with Et2O and dissolved in 70 cc. EtOH, and the solution cooled gave 12.8 g. monoformyl derivative (IX) of the 1-Me derivative (X) of VI, m. 210°; it gave recrystd. from aqueous EtOH a lower-melting hydrate, m. 188-9° with loss of moisture at 133-5°. VIII (2.0 g.) in 40 cc. 90% HCO2H hydrogenated in the usual manner and evaporated in vacuo, and the residual brown oil dissolved in a small amount of EtOH and cooled at 0° yielded 1.5 g. IX, m. 188-90°. IX (10 g.) recrystd. from 30 cc. 20% H2SO4 containing 25 cc. EtOH yielded 13.9 g. X.H2SO4, m. above 300°. 1-Phenyl-3-hydroxy-5-aminopyrazole (5.25 g.) in 50 cc. 10% aqueous NaOH added dropwise to PhN2Cl in NaOAc buffer (from 3 g. PhNH2, 6 cc. concentrated HCl, 2.1 g. NaNO2, and 12 cc. H2O) stirred 0.5 hr., and filtered gave 7.95 g. 1-Ph derivative (XI) of II, deep yellow plates, m. 266-8° (decomposition) (Cellosolve). 2-Phenyl-3-hydroxy-5-aminopyrazole yielded similarly 91% 2-Ph derivative (XII) of II, purple-red needles, m. 194-5° (EtOH). I (40 g.), 20 cc. PhNHNH2, and 200 cc. iso-AmOH refluxed 24 hrs., cooled to room temperature, and filtered, and the residue washed with 100 cc. cold EtOH gave 24.2 g. XII;

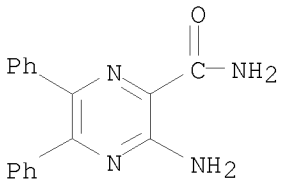
the mother liquor kept at 0° overnight deposited 1.8 g. phenylazomalonamide phenylhydrazone N-phenylhydrazide, yellow needles, m. 187-8° (EtOH). I (4 g.) and 2 cc. PhNHNH2 refluxed 20 hrs. with 0.87 g. Na in 75 cc. iso-AmOH and evaporated in vacuo, the residue triturated with 50% aqueous AcOH, the resulting solid extracted with 200 cc. boiling EtOH, and the extract concentrated to 50 cc. and cooled yielded 1.39 g. XII; the EtOH-insol. residue recrystd. from Cellosolve yielded 0.82 g. XI, m. 266-8° (decomposition). XI (5.0 g.) in 50 cc. 90% HCO2H hydrogenated 1 hr. at room temperature and 3 atmospheric over 0.5 g. 10% Pd-C, filtered, and evaporated in vacuo, and the oily residue triturated with 50 cc. 1:3 EtOH-Et2O gave 3.1 g. monoformyl derivative (XIII) of 1-phenyl-3-hydroxy-4,5-diaminopyrazole (XIV), plates, m. 223-5° (decomposition) (aqueous EtOH). Crude XIII (3.1 g.) warmed on a water bath with 3 cc. concentrated H2SO4, 7 cc. H2O, and 3 cc. EtOH, diluted with 4 cc. EtOH, and cooled gave 4.8 g. XIV.H2SO4, yellow needles. XII (8.0 g.), 100 cc. 90% HCO2H, and 0.8 g. 10% Pd-C hydrogenated at 3 atmospheric yielded 4.8 g. monoformyl derivative (XV) of 2-phenyl-3-hydroxy-4,5-diaminopyrazole (XVI), m. 235° (decomposition) (aqueous EtOH). XII (12 g.) converted to the XV and the crude product crystallized from 1:1 30% H2SO4-EtOH yielded 11.6 g. XVI.H2SO4, orange plates. VI.H2SO4 (20 g.) and 28 g. glyoxal-NaHSO3 adduct (XVII) in 250 cc. H2O treated dropwise with stirring at 60°, stirred 0.5 hr., adjusted to pH 5, cooled to 0°, and filtered gave 9.9 g. 3-hydroxy-1-pyrazolo[b]pyrazine (XVIII), yellow, m. 314-15° (decomposition). VI.H2SO4 (1.5 g.) in 10 cc. H2O treated with shaking with 1 cc. Ac2 and filtered yielded 0.93 g. 5,6-di-Me derivative (XIX) of XVIII, yellow, m. 325° (decomposition) (sublimed at 230°/0.1 mm.). VI.H2SO4 (4.2 g.), 6.3 g. Bz2, 1.2 g. NaOH, 30 cc. EtCOMe, 30 cc. EtOH, and 20 cc. H2O refluxed 1.5 hrs., concentrated in vacuo to about 1/6 its original volume, basified with aqueous NaOH, treated with C, and filtered, the filtrate acidified with HCl, and the precipitate repptd. from aqueous NaOH with HCl and dried azeotropically with C6H6 yielded 3.5 g. 5,6-di-Ph derivative (XX) of XVIII, yellow, m. 269° (decomposition) (EtOAc). X.H2SO4 (4.52 g.), 5.6 g. XVII, and 40 cc. H2O adjusted slowly with stirring to pH 5, kept at room temperature overnight, and filtered gave 2.84 g. 1-Me derivative (XXI) of XVIII, bright yellow needles, m. 242-3° (sublimed at 200°/0.1 mm.). XVIII (1.0 g.) in 10 cc. 10% aqueous NaOH treated at 60° with stirring with 1.4 g. MeI and evaporated in vacuo after 45 min., and the residue dissolved in a little H2O and repptd. with AcOH (pH 5) yielded 0.62 g. XXI. X.H2SO4 (1.13 g.), 0.5 cc. Ac2, and 10 cc. H2O treated dropwise with NH4OH to pH 7-8 and readjusted to pH 5 after 10 min. with AcOH gave 0.78 g. 1,5,6-tri-Me derivative of XVIII, m. 268-9° (EtOH and sublimed at 200°/0.1 mm.). X.H2SO4 (1.0 g.), 1 g. Bz2, 10 cc. H2O, 10 cc. EtAc, and 10 cc. EtOH adjusted to pH 8 with 40% aqueous NaOH, refluxed 1.5 hrs., kept at room temperature overnight, and concentrated in vacuo, the residue diluted with H2O, the suspension adjusted with NaOH to pH 9, and the solution heated to boiling, treated with C, filtered, and acidified with AcOH yielded 0.35 g. 1-Me derivative of XX, m. 258-60° (EtOH and sublimed at 200°/0.1 mm.). XVIII (15 g.) in 150 cc. 10% aqueous NaOH and 15 cc. EtOH treated with 15 cc. PhCH2Cl, evaporated after 1 hr. in vacuo, acidified with 50% aqueous AcOH, and filtered gave 18.4 g. 1-PhCH2 derivative (XXII) of XVIII, pale yellow needles, m. 175-6° (MeOH). XIV.H2SO4 (12 g.) and 13 g. XVII in 150 cc. H2O adjusted slowly with concentrated NH4OH to pH 7-8, stirred 45 min., readjusted to pH 5 with glacial AcOH, and cooled to 0° yielded 7.7 g. 1-Ph derivative (XXIII) of XVIII, lime-green needles, m. 227-9° (aqueous EtOH). XVI.H2SO4 (37 g.), 40 g. XVII, and 400 cc. H2O gave in the same manner 23.2 g. 2-phenyl-1-pyrazolo[b]pyrazin-3(2H)-

one (XXIV), pale green plates, m. 232-3.5° (EtOH). XVI.H2SO4 (0.96 g.), 0.4 cc. Ac2, and 100 cc. H2O yielded in the same manner 0.8 g. 5,6-di-Me derivative of XXIV, m. 239-40°, which recrystd. from EtOH and sublimed at 200°/0.1 mm. gave another polymorphic form, m. 193-5°. VI.H2SO4 (8.5 g.) and 8.8 g. NaHSO3 in 100 cc. H2O treated with 6 cc. 47.5% AcCHO, treated dropwise with stirring at 60° until the pH reached 7-8, stirred 45 min., adjusted with dilute AcOH to pH 4-5, and cooled to 0° gave 3.83 g. 6-Me derivative (XXV) of XVIII, light yellow needles, m. 319-21° (H2O); the mother concentrated in vacuo to 1/3 the original volume and kept 24 hrs. at 0° gave 1.15 g. 5-Me derivative (XXVI) of XVIII, buff-colored prisms, m. 234-5° (EtOH). XVIII (1.0 g.), 20 cc. HCONH2, and 3 g. Raney Ni heated 1.5 hrs. with stirring at 115-20°, treated with an addnl. 2 g. catalyst, heated again 1.5 hrs. with stirring, filtered, and cooled yielded 0.58 g. 2-aminopyrazine-3-carboxamide (XXVII), m. 244-5°. XIX (0.5 g.), 50 cc. 95% EtOH, and 6 g. Raney Ni refluxed 2 hrs., filtered, and evaporated, and the solid residue sublimed at 200°/0.1 mm. gave 0.28 g. 5,6-di-Me derivative (XXVIII) of XXVII, light yellow, m. 255°. IV (1.28 g.) in 40 cc. H2O containing 2 cc. concentrated NH4OH refluxed 7 hrs. with 1.2 g. Ac2 and 4 g. Raney Ni, filtered, and cooled to 0° gave 0.32 g. XXVIII; the Raney Ni residue extracted with boiling EtOH gave an addnl. 0.06 g. XXVIII. XX (1.0 g.), 50 cc. 95% EtOH, and 8 g. Raney Ni refluxed 3 hrs., filtered, and evaporated in vacuo, the residue triturated with H2O and filtered, and the insol. portion washed, dried (0.8 g.), and sublimed at 190°/0.01 mm. yielded the 5,6-di-Ph derivative of XXVII, bright yellow, m. 203-5°. XXI (1.0 g.), 100 cc. 95% EtOH, and 5 g. Raney Ni refluxed 2.5 hrs., filtered, and evaporated in vacuo gave 0.38 g. 2-MeNH analog of XXVII, light yellow rods, m. 200-1° (sublimed at 180°/0.1 mm.). XXIII (6 g.), 60 g. Raney Ni, and 600 cc. EtOH refluxed 4 hrs. with stirring and filtered through Celite, the filter cake extracted with hot EtOH, the combined filtrate and washing evaporated in vacuo, and the residue (3.2 g.) recrystd. gave the 2-PhNH analog of XXVII, greenish yellow plates from EtOH by slow crystallization or needles by rapid cooling, m. 175-6°. XXIV (5.0 g.), 500 cc. 95% EtOH, and 50 g. Raney Ni refluxed 3 hrs. and filtered, the residue washed with hot EtOH, the combined alc. solns. evaporated, and the residue sublimed at 160-70°/15 mm. yield 52% 2-aminopyrazine-3-carboxylic acid anilide (XXIX), needles, m. 106-7° (EtOH). XXIX (2.0 g.) and 50 cc. 10% aqueous NaOH refluxed 2.5 hrs., diluted with 50 cc. H2O, cooled, and extracted with Et2O, and the aqueous layer adjusted to pH 5 gave 2-aminopyrazine-3-carboxylic acid (XXX), m. 200-1°; the Et2O extract evaporated and the residual oil treated with Ac2O gave 0.41 g. AcNHPh, m. 112-13°. XXII (3.75 g.), 40 g. Raney Ni, and 400 cc. EtOH refluxed 3 hrs. with stirring gave in the usual manner 0.24 g. unchanged XXII and 1.35 g. 2-PhCH2NH analog (XXXI) of XXVII, needles, m. 125-6° (EtOH). XXXI (1.0 g.) and 10 cc. 10% aqueous NaOH refluxed 2 hrs., adjusted to pH 4 with dilute HCl, cooled, and filtered gave 0.78 g. 2-PhCH2NH derivative of XXX, plates, m. 166.5-68° (aqueous EtOH). XXVI (2 g.), 20 g. Raney Ni, and 200 cc. EtOH refluxed 4 hrs. with stirring gave 0.93 g. 5-Me derivative of XXVII, m. 203-4° (MeOH). XXV gave similarly 51.5% 6-Me derivative (XXXII) of XXVII, pale yellow, m. 235-6° (sublimed at 160-70°/18 mm.). XXXII (1.0 g.) and 10 cc. 10% aqueous NaOH refluxed 2 hrs., adjusted to pH 4 with dilute HCl, cooled to 0°, and filtered gave 0.72 g. 6-Me derivative of XXX, m. 211-12° (decomposition) (aqueous EtOH).

IT 101445-25-4P, Pyrazinamide, 3-amino-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)

RN 101445-25-4 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



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ACCESSION NUMBER: 1957:76968 CAPLUS
DOCUMENT NUMBER: 51:76968
ORIGINAL REFERENCE NO.: 51:13875a-h
TITLE: Pteridines. V. Derivatives of 1,4-dihydro-1- and 3,4-dihydro-3-methyl-6,7-diphenylpteridine
AUTHOR(S): Boon, W. R.; Bratt, G.
CORPORATE SOURCE: Imp. Chem. Ltd., Manchester, UK
SOURCE: Journal of the Chemical Society (1957) 2159-61
CODEN: JCSOA9; ISSN: 0368-1769
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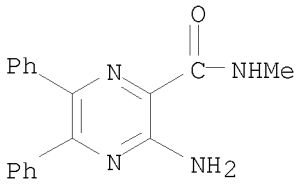
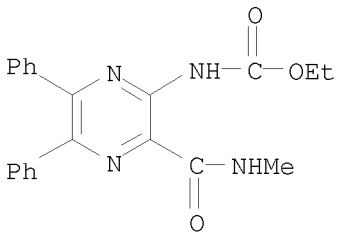
AB Condensation of MeHNC(:NH)NH2 with CH2CNCO2Et gave 4-amino-6-hydroxy-2-methylaminopyrimidine and 2,6-diamino-3,4-dihydro-3-methyl-4-oxopyrimidine and not 2,6-diamino-3,4-dihydro-3-methyl-4-oxopyrimidine (Roth, et al., C.A. 46, 3059g). 5,6-Diamino-1,4-dihydro-2-mercapto-1-methyl-4-oxopyrimidine sulfate (I) [Traube and Winter, Arch. Pharm. 244, 16(1906)] (7 g.), 6 g. benzil (II), and 18 g. NaOAc.3H2O (III) refluxed 6 hrs. in 75% aqueous EtOH, the mixture cooled, the product collected, extracted with hot petr. ether (b. 100-20°), and crystallized from BuOH gave 7.4 g. 1,4-dihydro-2-mercapto-1-methyl-4-oxo-6,7-diphenylpteridine (IV), m. 289°. 2,5,6-Triamino-1,4-dihydro-1-methyl-4-oxopyrimidine (6.3 g.), 5.8 g. II, and 17 g. III refluxed 6 hrs. in 25% aqueous EtOH, the solution cooled, the precipitate collected, and crystallized from HCONMe2 (V) gave 10 g. 2-amino-1,4-dihydro-1-methyl-4- oxo-6,7-diphenylpteridine (VI), m. 333° (decomposition). IV (0.4 g.), 0.5 g. HgO, 70 cc. BuOH, and 10 cc. CHCl3 refluxed 6 hrs. in a slow stream of NH3, the mixture filtered hot, the filtrate evaporated in vacuo, and the residue crystallized from V and then from EtOH gave VI, m. 333° (decomposition). 1,4-Dihydro-1-methyl-2-methylamino-4-oxo-6,7-diphenylpteridine (VII), m. 307° (from EtOH), was obtained similarly using MeNH2 in lieu of NH3. VI (0.5 g.) and 50 cc. 2N NaOH refluxed 4 hrs., the solution cooled, acidified with AcOH, the precipitate collected, and crystallized from aqueous EtOH gave 0.16 g. 1,4-dihydro-2-hydroxy-1-methyl-4-oxo-6,7-diphenylpteridine (VIII), m. 280°. To 0.9 g. I in N KOH was added dropwise with stirring at 100° 10 cc. H2O2 (100 volume), the solution cooled, acidified with AcOH, the precipitate (0.3 g.) collected, and crystallized from EtOH giving VIII, m. 280°. 2-Amino-1,4-dihydro-1-methyl-6,7-diphenyl-4-thionopteridine (IX) (see below) (3 g.) in 300 cc. 2N NaOH refluxed 4 hrs., the solution cooled, acidified, and the product fractionally crystallized from MeOH gave VIII. VI (15 g.), 19.5 g. P2S5, and 300 cc. pyridine (X) refluxed 2 hrs., X removed in vacuo, the residue extracted with 2% aqueous NaOH, and crystallized twice from V gave 7.4 g. IX, m. 295° (decomposition). On similar treatment, VII gave 16% 1,4-dihydro-1-methyl-2-methylamino-6,7-diphenyl-4-thionopteridine, m. 300° (decomposition) (from V), and IV gave 53% 1,4-dihydro-2-mercapto-1-methyl-6,7-diphenyl-4-thionopteridine, m. 375° (decomposition) (from V without prior extraction with NaOH). 2,4-Diamino-6,7-diphenylpteridine (3 g.), 6 g. MeI, and 60 cc. EtOCH2CH2OH refluxed 3 hrs., the solution cooled, the

hydriodide [m. 315° (decomposition)] collected, and boiled 5 min, with 10% aqueous Na2CO3 gave 1.7 g. 2-amino-1,4-dihydro-4-imino-1-methyl-6,7-diphenylpteridine (XI), m. 256 °. IX (2 g.), 2.5 g. HgO, 120 cc. EtOH, and 20 cc. CHCl3 refluxed 6 hrs. in a stream of NH3, the mixture filtered hot, the filtrate cooled, and the product (0.9 g.) crystallized from EtOH gave XI, m. 256°. Similarly was obtained 21% 2-amino-1,4-dihydro-1-methyl-4-methylimino-6,7-diphenylpteridine, m. 256° (from EtOH). 2-Amino-5,6-diphenylpyrazine-3-carboxylic acid (Weijlard, et al., C.A. 39, 30012) Me ester (3.6 g.) and 50 g. MeNH2 in 500 cc. EtOH heated 16 hrs. at 160-70°, the solution cooled, the precipitate collected, and crystallized from MeOH gave 2 g. N:C(NH2).C(CONHMe):NCPh:CPh.N (XII), m. 198°. XII (1.5 g.) and 40 cc. ClCO2Et refluxed 20 hrs., excess ClCO2Et removed in vacuo, and the residue crystallized from CHCl3-petr. ether gave 1.7 g. N:C(NHCO2Et).C(CONHMe):N.CPh:CPh.N (XIII), m. 153°. XIII (1.25 g.) refluxed 10 hrs. with NaOMe solution (from 1.5 g. Na in 200 cc. EtOH), EtOH removed in vacuo, the residue suspended in H2O, acidified with AcOH, and the precipitate crystallized from EtOH gave 0.7 g.
3,4-dihydro-2-hydroxy-3-methyl-4-oxo-6,7-diphenylpteridine, m. 307°.

IT 60980-98-5
(Derived from data in the 6th Collective Formula Index (1957-1961))
RN 60980-98-5 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-methyl-5,6-diphenyl- (9CI) (CA INDEX NAME)



IT 102318-77-4P, Pyrazinecarbamic acid, 3-methylcarbamoyl-5,6-diphenyl-, ethyl ester
RL: PREP (Preparation)
(preparation of)
RN 102318-77-4 CAPLUS
CN Pyrazinecarbamic acid, 3-methylcarbamoyl-5,6-diphenyl-, ethyl ester (6CI) (CA INDEX NAME)



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ACCESSION NUMBER: 1957:76967 CAPLUS
DOCUMENT NUMBER: 51:76967
ORIGINAL REFERENCE NO.: 51:13870c-i,13871a-i,13872a-i,13873a-i,13874a-i,13875a
TITLE: Pteridines. IV. Derivatives of 2,4-diaminopteridine and related compounds
AUTHOR(S): Boon, W. R.

CORPORATE SOURCE: Imp. Chem. Ltd., Manchester, UK
SOURCE: Journal of the Chemical Society (1957) 2146-58
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 51:76967
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 46, 2082g. Several derivs. of 2,4-(H2N)2-Y (in this abstract Y = pteridine) possess antimalarial activity (Potter and Henshall, C.A. 51, 1974h). A series of 2,4,6,7-(H2N)2Ph2-Y were prepared in which the H2N groups were progressively substituted by Me. Antimalarial activity was immediately lost, but the compds. were active against exptl. schistosomiasis in mice. Further modifications of the substituents always lowered the activity. Only a few compds. showed any appreciable activity. 2,4,6-Me2N-(HO)2-Z (in this abstract Z = pyrimidine) ground to pass a 30-mesh sieve, added with stirring during 45 min. to 280 cc. AcOH and 65 cc. HNO3 (d. 1.5) at 20-5°, stirred an addnl. 45 min., the mixture poured into 1350 cc. H2O, the solid separated, washed free from acid, and dried gave 81 g. 5-O2N derivative (I). I (5 g.), 60 cc. POCl3, and 20 cc. PhNMe2 heated to 105° (bath temperature), after the vigorous reaction the heating continued 1 hr., excess POCl3 removed in vacuo, the residue treated with 200 g. ice, the suspension extracted with four 50-cc. portions of Et2O, the combined exts. dried, filtered, evaporated, and the residue crystallized from petr. ether (b. 60-80°) gave 3.7 g. 4,6-Cl2 compound (II), m. 117-20°. II (14 g.), 90 cc. C6H6, and 10 cc. aqueous NH3 (d. 0.880) shaken overnight, the mixture filtered, and the residue (4.2 g.) crystallized twice from dioxane gave the 4,6-(H2N)2 compound, m. 249-50°; evaporation of the filtrate gave a residue which, after chromatography on 120 g. Al2O3 in 30 cc. C6H6 and crystallization from EtOAc-petr. ether afforded 0.5 g. 4-H2N compound, m. 132°. To 91 g. Na in 2 l. MeOH was added 509 g. [MeHNC(:NH)NH2]2.H2SO4, the mixture refluxed 30 min. with stirring, CH2(CO2Et)2 added, the heating continued 6 hrs., the mixture cooled, diluted with 5 l. H2O, treated with C, filtered, the filtrate acidified to litmus with AcOH, and the precipitate collected to give 183 g. 2,4,6-MeHN(HO)2-Z (III); the mother liquors deposited 15 g. presumably 2-amino-1,4,5,6-tetrahydro-1-methyl-4,6-dioxo-Z, m. above 360°. III (93g.) and 510 g. POCl3 refluxed 1 hr., the mixture filtered through sintered glass, the filtrate poured on 2250 cc. 32% aqueous NaOH and ice, the separated solid collected, washed with H2O, and crystallized from MeOH gave 88 g. 2,4,6-(MeHN)Cl2-Z (IV), m. 164°. IV (130 g.) heated 12 hrs. with NaOMe (from 168 g. Na in 570 cc. MeOH), the solution cooled, the precipitate collected, washed with H2O, and crystallized from MeOH yielded 95 g. 4,6,2-Cl(MeO)(MeHN)-Z, m. 153°. Similarly was prepared 81% 4,6,2-Cl(MeO)(Me2N)-Z (VI), m. 62° (after sublimation at 55°/0.1 mm.), from 4,6,2-Cl2(Me2N)-Z at room temperature VI (10 g.) heated 30 min. on a steam bath with 50 cc. HCl, the solution cooled, the product collected, and purified by solution in aqueous alkali, treatment with C, and repptn. with AcOH gave 5.5 g. 6-HO compound, m. 265° (decomposition). Similarly was obtained from VI 95% 4,6,2-Cl(HO)(Me2N)-Z (VII), m. 217°. 4,6,2-ClMe(H2N)-Z (28.7 g.) and 78 cc. 19.5% alc. Me2NH heated 17 hrs. at 110-20° gave 172 g. 4-Me2N derivative, m. 172° (from C6H6). Ph(H2N)CHCOPh.HCl (47 g.) dissolved in 750 cc. H2O. basified at 0° with aqueous NH3, the base collected, sucked as dry as possible, added to 35 g. 2,4,6-Cl3-Z (VIII) in 750 cc. EtOH, the mixture set aside 2 days at room temperature, the precipitate (12 g.) collected, and crystallized from EtOH gave α-(2,4-dichloro-6-pyrimidylamino)deoxybenzoin (IX), m. 165°. p-ClC6H4CHBzNH2 (X) (28.5 g.) converted to the base, the latter treated as above with 9 g. VIII, the crude product refluxed 3 hrs. with 10 cc. 19.5% alc. Me2NH and

10 cc. EtOH, the solution evaporated to 0.5 its volume, and the solid recrystd. from MeOH gave ω-(4-chloro-2-dimethylamino-6-pyrimidyl-amino)-ω-(p-chlorophenyl)acetophenone, m. 151-2°; the mother liquors gave the 6-Me2N isomer, m. 181-2° (from EtOH), and a small amount of another compound believed to be 2,5-di(p-chlorophenyl)-3,6-diphenylpyrazine, m. 239-40°. 4,6,2-Cl2(H2N)-Z (XI) (33 g.) heated 3 hrs. with 175 cc. 19.5% alc. Me2NH, after the initial reaction had subsided the solution cooled, the precipitate (24 g.) collected, and crystallized from MeOH and then from C6H6 gave 4,2,6-Cl(H2N)(Me2N)-Z, m. 164-5°. Similarly were obtained in 70% yield from the appropriate derivative of XI and an alc. solution of H2NCH2CO2Et, Et 4-chloro-2-methylamino-6-pyrimidylaminoacetate (XII), m. 167°, and Et 4-chloro-2-dimethylamino-6-pyrimidylamino-acetate, m. 121°. 2,4,6-Cl2(Me2N)-Z (36 g.), 200 cc. EtOH, and 50 cc. 70% aqueous EtNH2 refluxed 6 hrs., EtOH removed, the mixture diluted with H2O, extracted with Et2O, the extract dried, Et2O removed, the residue dissolved in 70 cc. absolute EtOH, 9 cc. concentrated H2SO4 added (the mixture acid to Congo red), and dry Et2O added to a permanent turbidity gave 34 g. 4,6,2-Cl(EtNH)(MeNH)-Z sulfate, m. 148° (from EtOH-Et2O). The following compds. were prepared similarly: 4,2,6-Cl(Me2N)(MeNH)-Z, m. 78° (from petr. ether); 4,2,6-Cl(Et2N)(MeNH)-Z sulfate, m. 148-9° (from EtOH-Et2O); 4-chloro-6-methylamino-2-piperidino-Z, m. 118° (from MeOH); 4,6,2-Cl(MeNH)(Me2NCH2CH2NH)-Z, m. 99° (from EtOAc-petr. ether).

To 17.5 g. VII in 500 cc. H2O containing 60 cc. 2N NaOH and 12.6 g. NaHCO3 was added 4-ClC6H4N2Cl (XIII) [from 12.75 g. 4-ClC6H4NH2 (XIV)], the solution stirred overnight, the precipitate collected, washed with H2O, EtOH, and Et2O, and crystallized from dioxane to give 20 g. 5-p-ClC6H4N2 derivative (XV), m. 220-2° (decomposition). 4,6,2,5-Cl(HO)(MeNH)(p-ClC6H4N2)-Z was obtained similarly but could not be purified without decomposition XIII (500 cc. 0.025M) and 46 g. NaOAc.3H2O (XVI) added with stirring to 3.8 g. 6,4,2-Me(HO)(Me2N)-Z in 500 cc. H2O, after 16 hrs. the precipitate collected, washed, dried in air, and recrystd. from BuOH gave 5.5 g. 5-(p-ClC6H4N2) derivative, m. 216-17°. XIII (50 cc. 0.025M) and 40 g. XVI added with stirring to 5.0 g. 4,2,6-Cl(Me2N)2-Z in 70 cc. AcOH, diluted with 200 cc. H2O, after 48 hrs. stirring the solid collected, washed with H2O, and crystallized twice from EtOH gave 5 g. 5-(p-ClC6H4N2) derivative (XVII), m. 91°. The following N.CX:N.CW:C(N:NR).CY (XVIII) (W = Cl) were prepared (X, Y, R, m.p., crystallization solvent, % yield given): NH2, NHMe, p-ClC6H4, 255°, HCONMe (XIX), 47; NH2, NMe2, p-ClC6H4, 204°, XIX-EtOH, 65; NHMe, NH2, p-ClC6H4, 272° (decomposition), XIX, 90; NHMe, NHMe, p-ClC6H4, 272°, XIX-EtOH, 95; NHEt, NHMe, p-ClC6H4, 214°, BuOH, 75; NMe2, NH2, p-ClC6H4, 229°, BuOH, 90; NMe2, NHMe, Ph, 163°, EtOH, 78; NMe2, NHMe, p-ClC6H4, 183°, BuOH, 90; HNCH2CH2NMe2, NHMe, p-ClC6H4, 158°, EtOH, 50.

6,4,2,5-Cl(H2N)(Me2N)(p-ClC6 H4N2)-Z (XX) (2 g.) and 40 cc. saturated alc. NH3 heated 36 hrs. at 150-60°, the solution cooled, and the product (1.75 g.) crystallized from BuOH gave 6-H2N compound, m. 272-3° [HCl salt, m. 301° (decomposition) (from 80% HCO2H) (prepared from XIII and 4,6,2-(H2N)2(Me2N)-Z in AcOH)]. Similarly were prepared the following XVIII (W = NH2, R = p-ClC6H4) (X, Y, m.p., crystallization solvent, % yield given): NH2, NHMe, 213°, BuOH, 40 and 80; NH2, NMe2, 205°, XIX-H2O, 96; NH2, NH(CH2)3NEt2, 139°, EtOH-H2O, 44; NHMe, NH2, 241°, BuOH, 70; NHMe, NHMe, 197°, EtOAc, 85 and 92; NHMe, NMe2, 184°, XIX-H2O, 90 and 79; NHEt, NHMe, 161°, BuOH, 80; NMe2, NHMe, 193°, BuOH, 90; NMe2, NMe2, 203°, BuOH, 95 and 93; NMe2, piperidino, 175°, BuOH, 86; NMe2, morpholino, 183°, BuOH, 91; NMe2, NH(CH2)2NEt2, 150°, petr. ether, 44; NH(CH2)2NMe2, NHMe, 144°, petr. ether, 90. XVII (5 g.), 100 cc. XIX, and 20 cc.

10% alc. NH3 heated 64 hrs. at 60°, H2O added, and the precipitate crystallized from EtOH gave 4 g. 4-Me2N derivative (XXI). m. 145°. XXI was also obtained similarly from XVII and MeOH-Me2NH. Similarly were prepared: 2,4,6,5-(H2N)(Me2N)(MeHN)(p-ClC6H4N2)-Z, m. 192°, and 2,4,6,5-(MeHN)3(p-ClC6H4N2)-Z, m. 155°. 2,4,6,5-(H2N)2(MeHN)(p-ClC 6H4N2)-Z (5 g.) in 75 cc. EtOH reduced by H over Raney Ni (initial pressure 47 atmospheric) at 90-5° 5 hrs., the mixture acidified with 4 cc. AcOH, filtered through Hyflo Supercel, the residue washed with H2O, the combined filtrate and washings evaporated to dryness in vacuo under N, the residue triturated with Et2O, dissolved in 10 cc. H2O, acidified to Congo red with H2SO4, EtOH added, and the precipitate crystallized from H2O gave 2,4,5,6-(H2N)3(MeHN)-Z sulfate (XXII). No satisfactory analytical results were obtained for 2,5,6,4-(H2N)2(Et2N)(Me2N)-Z oxalate, m. 221° (decomposition), but it condensed normally with benzil to the pteridine. The following XC:N.C(NH2):C(NH2).CY:N were prepared (X, Y, m.p., crystallization solvent, % yield given): NH2, NHMe, 250° (decomposition), H2O, 89; NH2, NMe2, 209°, aqueous EtOH, 48; NHMe, NH2, 255° (decomposition), H2O, 75; NHMe, NHMe, 259°, aqueous EtOH, 80; NHMe, NMe2, 193°, aqueous EtOH, 65; NHEt, NHMe, 293° (decomposition), aqueous EtOH, 49; NMe2, NH2, 314° (decomposition), H2O, 58; NMe2, NHMe, 273° (decomposition), H2O, 64; NMe2, NMe2, 182° (decomposition), EtOH, 38; NMe2, piperidino, 208° (decomposition), aqueous EtOH, 33; NMe2, morpholino, 194° (decomposition), aqueous EtOH, 57. H2NCH2CH(OEt)2 (15 g.) and 17.5 g. 6,4,2,5-Cl(MeHN)-(Me2N)(p-ClC6H4N2)-Z refluxed 24 hrs. in dioxane, the solution evaporated to dryness, the residue (10 g.) triturated with EtOH, filtered off, and crystallized from petr. ether gave 5-p-chlorophenylazo-2-dimethylamino-4-methylamino-6-pyrimidylaminoacetaldehyde di-Et acetal, m. 95°. PhCH(NH2)CH(OMe)2 (XXIII) (11 g.) and XVII in 205 cc. dioxane refluxed 4 hrs., the solvent removed, and the product (1.9 g.) crystallized from BuOH gave α-[5-p-chlorophenylazo-2,4-bis(dimethylamino)-6-pyrimidyl]amino-α-phenylacetaldehyde di-Me acetal, m. 151°. Similarly was prepared from XV α-(5-p-chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidyl)-amino-α-phenylacetaldehyde di-Me acetal (XXIIIa), m. 242° (from BuOH). H2NCH2C(:NNHCONH2)Me.HCl (11 g.) stirred 2 hrs. with cold NaOEt (from 1.5 g. Na in 60 cc. EtOH), 9.3 g. XV in 140 cc. XIX added, stirring continued 15 hrs., the semicarbazone, m. 243°, collected, washed with H2O and EtOH, dissolved in 25 cc. AcOH and 150 cc. 2N aqueous HCl, the solution kept overnight, filtered, the filtrate evaporated to dryness, and the residue (6.6 g.) crystallized from EtOH gave 5-p-chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylaminoacetone HCl salt, m. 217°. The following compds. were prepared similarly: ω-(5-p-chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidyl)aminoacetophenone (XXIV) HCl salt monohydrate, m. 229° (from EtOH) [XXIV semicarbazone, m. 263° (decomposition) (from XIX-EtOH)]; 4-chloro-ω-(5-p-chlorophenylazo-4-hydroxy-2-methylamino-6-pyrimidyl)aminoacetophenone (XXIVa), m. 258° (decomposition) [semicarbazone, m. 264° (from XIX)]; 4'-Cl derivative of XXIV, m. 244° (decomposition) (from XIX-EtOH) [semicarbazone, m. 255° (decomposition) (from XIX-EtOH)]. IX (17.5 g.) and 60 cc. 2.5M alc. Me2NH refluxed 3 hrs., cooled, the solid (17 g.) collected, dissolved in 200 cc. AcOH together with 19 g. XVI, a solution of XIII (from 6 g. XIV) added, after stirring 4 days the resulting precipitate collected, washed with H2O and EtOH, and crystallized from BuOH gave 10 g. α-(4-chloro-5-p-chlorophenylazo - 2 - dimethylamino-6-pyrimidyl)aminodeoxybenzoin (XXV), m. 254° (decomposition). XXV (10 g.) refluxed 20 hrs. with 340 cc. 2.5M alc. Me2NH gave 5.5 g. 4-Me2N derivative, m. 179° (from EtOH). The following compds. were prepared similarly: ω-(p-chlorophenyl)-ω-(4-chloro-5-p-chlorophenylazo-2-dimethylamino-6-pyrimidyl)aminoacetophenone, m. 248° (decomposition) (from BuOH), and ω-(p-chlorophenyl)-ω-(5-p-chlorophenylazo-2-dimethylamino-6-pyrimidyl)aminoacetophenone, m. 196° (from BuOH). 4-ClC6H4COCH(NH2)Ph.HCl (14.1 g.) dissolved in 800 cc. H2O, made alkaline with aqueous NH3, the base collected, dried over P2O5,

added to 7.8 g. XV in 400 cc. XIX, the mixture stirred 24 hrs. at room temperature, the solid collected, and crystallized from XIX-EtOH gave 7 g. 4-chloro-ω-(5-p-chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidyl)amino-ω-phenylacetophenone, m. 239°. To 5.6 g. H2NCH2CO2Et was added 5.5 g. IX in 150 cc. dioxane, the whole refluxed 8 hrs., cooled, filtered, the filtrate diluted with H2O, the precipitate collected, crystallized from EtOAc-petr. ether, and recrystd. from EtOH to give 2 g. Et (4-amino-5-p-chlorophenylazo-2-dimethylamino-6-pyrimidyl)aminoacetate, m. 139°. (For addnl. compds. of this type, cf. Brit. 763,043). Similarly was prepared Et (5-p-chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidyl)-aminoacetate, m. 218°. A solution (17 cc. 0.01 M) of XIII added to 2.5 g. XII in 160 cc. 50% AcOH containing 10 g. XVI, the whole stirred 12 hrs., the precipitate collected, and crystallized from BuOH gave 2 g. Et (4-chloro-5-p-chlorophenylazo-2-methylamino-6-pyrimidyl)aminoacetate, m. 218°. Similarly was prepared Et (4-chloro-5-p-chlorophenylazo-2-dimethylamino-6-pyrimidyl)aminoacetate, m. 214° (from dioxane). ω-(5-p-Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidyl)-aminoacetophenone (1.2 g.)in 60 cc. AcOH treated at the b.p. with 1.1 g. Zn dust in an N atmospheric, the mixture heated 1 hr. more, filtered hot, the filtrate evaporated in vacuo, the residual oil triturated with Et2O, filtered, the residue washed with Et2O, dissolved in dilute HCl, the solution evaporated in vacuo, the residue triturated with EtOAc, collected, dissolved in H2O, the solution made alkaline with aqueous NH3, and the product (0.1 g.) crystallized from EtOH gave 2-dimethylamino-7,8-dihydro-4-hydroxy-6-phenyl-Y-0.5 H2O (XXVI), m. 311°, λ 270 mμ (E1cm.1% 750 in N HCl). Similarly were prepared the following compds.: 2,4-bis(dimethylamino)-7,8-dihydro-6,7-diphenyl-Y, m. 278°; 7-p-chlorophenyl-2-dimethylamino-6,7-dihydro-4-methylamino-6-phenyl-Y, m. 267-9° (not analytically pure); 6-p-chlorophenyl-2-dimethylamino-7,8-dihydro-4-hydroxy-7-phenyl-Y HCl salt, m. 346°. XXIVa (2.95 g.) in 300 cc. XIX shaken in H (initial pressure 2 atmospheric) 2 hrs. with 5 g. Raney Ni, the catalyst and XIX removed, the residue triturated with Et2O, the solid collected, and recrystd. from aqueous XIX gave 1.8 g. 6-p-chlorophenyl-2-dimethylamino-7,8-dihydro-4-hydroxy-Y, m. 370°. XXIIIa (5 g.) treated with 10 cc. concentrated HCl in 100 cc. AcOH, after 1 hr. at room temperature H2O added, the precipitate collected, reduced with H over Raney Ni, the catalyst and solvent removed, the oily residue mixed with 10 cc. AcOH, triturated twice with Et2O, the remaining oil dissolved in 2N HCl, the resulting solid suspended in H2O, treated with dilute aqueous NH3 until the mixture was just alkaline to Brilliant Yellow, the precipitate (2.3 g.) collected, and crystallized from aqueous XIX gave 7,4,2-Ph(HO)(Me2N)-Y, m. 326° (decomposition), λ 355 mμ (E1cm.1% 800, in N HCl). 6,4,5,2-HO(H2N)2(Me2N)-Z sulfate (XXVII) (10.7 g.), 6.1 g. PhCOCHO.H2O, 27 g. XVI, and 400 cc. 50% aqueous EtOH refluxed 15 min., the mixture cooled, the solid collected, and crystallized from EtOH gave 7.5 g. 6,4,2,5-HO(H2N)(Me2N)(PhCOCH:N)-Z, m. 267° (decomposition). Me 3-amino-5,6-diphenylpyrazine-2-carboxylate (1 g.) heated 16 hrs. at 160° with 10 g. MeNH2 in 55 cc. EtOH gave 0.5 g. 2-amino-3-N-methylcarbamoyl-5,6-diphenylpyrazine, 197-8° (from EtOH). 2,4-Disubstituted pteridines were prepared by the following methods (for addnl. compds., cf. Brit. 763,044, C.A. 51, 13944a): (1) To 0.2 g. XXVI in 50 cc. 0.5N NaOH was added 0.1 g. KMnO4 in 15 cc. H2O with stirring over 15 min., after a further 1.5 hrs. EtOH added, MnO2 filtered off, washed with H2O, the filtrate and washings concentrated to about 50 cc., acidified to Congo red with HCl, neutralized with aqueous NH3, and the product

crystallized from EtOH gave 6,4,2-Ph(HO)(Me2N)-Y (XXIX), m. 322° (decomposition), λ 280 (E1cm.1% 910), 355 mμ (E1cm.1% 395). (2a) 4,5,2,6-(H2N)2(Me2N)2-Z sulfate (2.94 g.), 6.8 g. XVI, 1.5 g. XXVIII, and 50% aqueous EtOH-refluxed 15 min., the solution cooled, the solid collected, dissolved in 2N AcOH, the solution treated with C, filtered, the filtrate made alkaline with aqueous NH3, and the precipitate crystallized from BuOH and then from EtOH gave 7,2,4-Ph(Me2N)2-Y, m. 191°. (2b) XXVII (7.43 g.), 250 cc. 6N H2SO4, 3.7 g. XXVIII, and 250 cc. EtOH refluxed 2 hrs., EtOH removed in vacuo, the residual solution cooled in ice, made alkaline with aqueous NH3, filtered, the filtrate acidified to litmus with dilute AcOH, and the precipitate crystallized from XIX-EtOH gave 6,4,2-Ph(HO)(Me2N)-Y, m. 332°. (2c) XXII (10.8 g.), 14.8 g. benzil, 24 g. XVI, 400 cc. EtOH, and 100 cc. H2O refluxed 5 hrs., the mixture cooled, the precipitate collected, extracted with 0.5N HCl, and the extract basified with aqueous NH3 gave 6,7,2,4-Ph2(H2N)(Me2N)-Y (XXX), m. 272° (from EtOH). (3) 6,7,4,2-Ph2(HO)(H2N)-Y (XXXI) (2 g.) and 120 cc. redistd. POCl3 refluxed 2 hrs., excess POCl3 removed in vacuo, the residue heated 1 hr. with 100 cc. 2.5 M alc. MeNH2, the alc. removed, the solid extracted with 0.5N HCl, and the extract basified with aqueous NH3 and crystallized from EtOH gave XXX, m. 272°. In a similar series of reactions, XXIX yielded 6,2,4-Ph(Me2N)2-Y, m. 190°, and 6,4,2-Ph(EtO)(Me2N)-Y, m. 200° (from EtOH). By using the conditions of Cain, et al. (C.A. 43, 4268e), there was obtained from XXXI a product (XXXII), m. 253-9°.

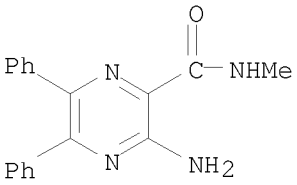
XXXII extracted with 1.5N AcOH left 2-amino-3-N-methylcarbamoyl-5,6-diphenylpyrazine, m. 197-8°; the extract basified with aqueous NH3 and the precipitate crystallized from EtOH gave 6,7,2,4-Ph2(Me2N)2-V (XXXIII), m. 266-7°, undepressed with material obtained by condensing 4,5,2,6-(H2N)2(MeHN)2-Z with benzil. 6,7,2,4-Ph2(HS)(H2N)-Y (XXXIV) treated with alc. MeNH2 under the conditions described by Taylor and Cain (C.A. 47, 137h) also gave XXXIII. XXXIV and alc. Me2NH similarly treated gave a product (XXXV), m. 186-215°. XXXV triturated with cold 0.5N AcOH left a residue which, when repeatedly crystallized from MeOH, m. 211°, undepressed with authentic 6,7,2,4-Ph2(Me2N)2-Y obtained by condensing 4,5,2,6-(H2N)2-(Me2N)2-Z with benzil; the acid extract basified with aqueous NH3, and the precipitate crystallized from BuOH gave 6,7,4,2-Ph2(H2N)(Me2N)-Y, m. 236°, undepressed with material obtained by condensing 4,5,6,2-(H2N)3(Me2N)-Z with benzil (4) 7,2,4-Ph(MeHN)2-Y (0.3 g.) and 50 cc. N HCl refluxed 20 hrs., the solution cooled to 50°, made faintly alkaline to Brilliant Yellow with aqueous NH3, the precipitate collected, washed with H2O, dried, and crystallized from XIX gave 7,4,2-Ph(HO)(MeHN)-Y, m. 387° (decomposition), undepressed with material prepared by 2a, λ 250 mμ (E1cm.1% 700). The following substituted pteridines, N:CX.N:CY.C:C.N:CR.CR':N, were prepared (X, Y, R, R', m.p., crystallization solvent, method of preparation, % yield given): NH2, NHMe, H, H, 248° H2O, 2c, 26; NH2, NHMe, Ph, Ph, 272°, EtOH, 2c and 3, 73.5; NH2, NMe2, Ph, Ph, 322° (decomposition), XIX, 2c, 63; NH2, NH(CH2)3-NEt2, Ph, Ph, 201°, EtOH, 2c, 50; NHMe, OH, Ph, H, 356° (decomposition) [λ 280 mμ (E1cm.1% 966), 350 mμ (E1cm.1% 566)], XIX, 2b, 75; NHMe, OH, H, Ph, 387° (decomposition), XIX, 2a and 4, 80 and 52; NHMe, OH, p-ClC6H4, H, 370° (decomposition), XIX-EtOH, 1 and 2b, 50 and 26; NHMe, OH, H, p-ClC6H4, 363° (decomposition), XIX, 2a and 4, 65 and 80; NHMe, OH, Ph, Ph, 365° (decomposition), XIX, 4, 80; NHMe, NH2, H, H, 242°, H2O, 2c, 72; NHMe, NH2, Me, Me, 281°, EtOH, 2c, 51; NHMe, NH2, Ph, Ph, 307°, XIX, 2c, 75; NHMe, NHMe, H, H,

214°, EtOH, 2c, 50; NHMe, NHMe, Me, Me, 266°, EtOH, 2c, 28; NHMe, NHMe, Ph, H, 264°, XIX, 3, 32; NHMe, NHMe, H, Ph, 256° [λ 365 mμ (E1cm.1% 950)], MeOH, 2b, 30; NHMe, NHMe, H, p-ClC6H4,294° [λ 365 mμ (E1cm.1% 925)], XIX, 2b, 25; NHMe, NHMe, Ph, Ph, 262°, XIX-EtOH, 2c, 49; NHMe, NHMe, o-ClC6H4, o-ClC6H4, 265°, BuOH, 2c, 22; NHMe, NHMe, m-ClC6H4, m-ClC6H4, 256°, MeOH, 2c, 31; NHMe, NHMe, p-ClC6H4, p-ClC6H4, 323° XIX, 2c, 63; NHMe, NHMe, p-MeOC6H4, p-MeOC6H4, 259°, EtOH, 2c, 24; NHMe, NHMe, 3,4-CH2O2C6H3, 3,4-CH2O2C6H3, 297°, XIX-EtOH, 2c, 28; NHMe, NHMe, R and R' = 9,10-phenanthrylene, 311°, XIX, 2c, 66; NHMe, NHMe, R and R' = 7,8-acenaphthylene, 307°, XIX, 2c, 40; NHMe, NHMe, 2-furyl, 2-furyl, 218°, EtOAc, 2c, 24; NHMe, NHMe, R and R' = 2,3-indolo, 338°, XIX, 2c, 75; NHMe, NMe2, Ph, Ph, 306°, XIX, 2c, 60; NHEt, NHMe, Ph, Ph, 249°, EtOH, 2c, 21; NMe2, OH, ph, H, 336° (decomposition), EtOH, 1, 2a, and 4, 15 and 90; NMe2, OH, H, Ph, 325° (decomposition), XIX-EtOH, 1, 2b, and 4, 65, 90, and 90; NMe2, OH, p-ClC6H4, H, 377° (decomposition), XIX-EtOH, 1, 85; NMe2, OH, Ph, Ph, 361°, XIX-EtOH, 2c, 33; NMe2, OH, p-ClC6H4, Ph, 350°, BuOH, 1, 85; NMe2, OEt, Ph, H, 200°, MeOH, EtOH on 4-Cl compound, 30; NMe2, NH2, Ph, Ph, 239°, BuOH, 2c, 63; NMe2, NHMe, Ph, Ph, 205°, EtOAc, 2c, 43; NMe2, NHMe, Ph, p-ClC6H4, 239° EtOH, 1, 70; NMe2, NMe2, iso-Pr, iso-Pr, 150°, aqueous EtOH, 2c, 30; NMe2, NMe2, Ph, H, 188°, EtOH, 2a and 3, 29 and 40; NMe2, NMe2, H, Ph, 191°, EtOH, 2b and 3, 37 and 80; NMe2, NMe2, Ph, Ph, 211°, EtOAc, 2c, 55; NMe2, piperidino, Ph, Ph, 207°, aqueous EtOH, 2c, 75; NMe2, morpholino, Ph, Ph, 216°, EtOH, 2c, 71. To a solution of PhCH:CHOAc in 290 cc. CCl4 was added 39 cc. Br in 40 cc. CCl4 with stirring below 10° during 1.5 hrs., 290 cc. MeOH added, stirring continued 12 hrs. more below 10°, after a further 48 hrs. the mixture poured into ice H2O, the separated oil collected, washed with 5% aqueous NaHCO3, dried, and distilled in the presence of a little Na2CO3 to give 122 g. PhCHBrCH(OMe)2 (XXXVI), b14 138-40°. XXXVI (122 g.), 183 g. PhCH2NH2, and a trace of NaI heated 1 hr. at 140°, when the reaction had moderated heating continued 2 hrs., the mixture cooled, poured into H2O, the product extracted with Et2O, the extract dried, and rectified gave 89 g. PhCH(CH2Ph) CH(OMe)2 (XXXVII), b0.2 121-48°. XXXVII hydrogenated in 300 cc. MeOH over 25 g. 5% Pd-C at 100-5° with an initial pressure of 95 atmospheric, the catalyst removed, and the filtrate rectified gave 47 g. XXIII, b18, 134-6°. BzCH2NH2.HCl (56 g.) dissolved in 350 cc. EtOH with gentle warming, the solution cooled rapidly to room temperature, 25 g. NH2NHCONH2 added, the mixture set aside several hrs., the crystals filtered off, and crystallized from EtOH gave the semicarbazone, m. 107-8°. To 28 g. 4-ClC6H4CH2Bz in 50 cc. dry Et2O saturated with HCl at 0° was added 7.5 g. BuNO2 in 50 cc. Et2O, the precipitate collected, and crystallized from aqueous MeOH giving the hydroxyimino compound (XXXVIII), m. 121-3°. XXXVIII reduced at room temperature and pressure in 350 cc. EtOH containing 12 cc. concentrated HCl over Pd-C, the catalyst and solvent removed, and the product (6 g.) crystallized from 2N HCl and then from MeOH-Et2O gave X, m. 248° (decomposition).

IT 60980-98-5P, Pyrazinamide, 3-amino-N-methyl-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)

RN 60980-98-5 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-methyl-5,6-diphenyl- (9CI) (CA INDEX NAME)




L7 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1957:76966 CAPLUS
DOCUMENT NUMBER: 51:76966
ORIGINAL REFERENCE NO.: 51:13869d-i,13870a-c
TITLE: Syntheses in the quinazolone series. VI. Synthesis of 1,2,3,4-tetrahydro-2-aryl-4-oxoquinazolines
AUTHOR(S): Kilroe Smith, T. A.; Stephen, Henry
CORPORATE SOURCE: Univ. Witwatersrand, Johannesburg, S. Afr.
SOURCE: Tetrahedron (1957), 1, 38-44
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 51:76966

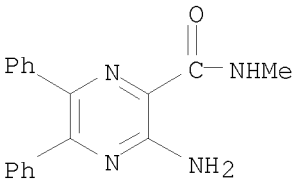
AB cf. C.A. 51, 9626b. N2-Arylideneorthoanilamides (o-arylideneaminobenzamides) (I), readily prepared by condensation of aromatic aldehydes with o-H2NC6H4CONH2, are characterized by the ease with which they isomerize to 1,2,3,4-tetrahydro-2-aryl-4-oxoquinazolines (II). The aromatic aldehyde (1 mole) and 1 mole o-H2NC6H4CONH2 refluxed in EtOH, the solution cooled, filtered, and the product crystallized from EtOH gave the following I (aryl group, m.p., and % yield given): o-HOC6H4, 165°, 81; o-MeOC6H4, 159°, 77; m-HOC6H4, 146°, 70; p-HOC6H4, 160°, 70; p-MeOC6H4, 158°, 61; 2,4-(HO)2C6H3, 190°, 90; 2,4-(MeO)2C6H3, 160°, 88; 2,4-(EtO)2C6H3, 177°, 87; 2,4-EtO(HO)C6H3, 180°, 72; 2,4-HO(EtO)C6H3 (Ia), isomerized, 66; 3,4-HO(MeO)C6H3 (Ib), 153°, 50; 3,4-MeO(HO)C6H3 (Ic), 187°, 81; 3,4-EtO(HO)C6H3, 187°, 97; 3,4-(MeO)2C6H3, 165°, 84; 3,4-EtO(MeO)C6H3, 152°, 60; 2,3-HO(MeO)C6H3, 168°, 81; o-O2NC6H4, 174°, 86; m-O2NC6H4, 199°, 95; p-O2NC6H4, 191°, 93; PhCH:CH, 210°, 90; and 2,3,4-HO2C(MeO)2C6H2, 208°, 96. Ia, Ib, and Ic isomerized during recrystn. from EtOH and were alkylated for identification and analysis. The I refluxed 30 min. with N HCl, then with 2N NaOH containing EtOH, or heated above the m.p. in vacuo in some instances gave good yields of the II [aryl, m.p., and % yield from the acid (a), base (b), or by heating (c) given]: Ph, 228°, -; p-MeC6H4, 230°, -; o-HOC6H4, 300°, 82a; m-HOC6H4, 209°, 100b; p-HOC6H4, 332°, 70a; o-MeOC6H4, 181°, 88b; p-MeOC6H4, 195°, 62a; 2,4-HO(EtO)C6H3, 305°, 100c; 2,4-(EtO)2C6H3, 149°, 94b; 2,4-(MeO)2C6H3, 187°, 100b; 2,3-HO(MeO)C6H3, 279°, 87a; 3,4-MeO(HO)C6H3, 224°, 92a; 3,4-HO(MeO)C6H3, 191°, -; 3,4-EtO(MeO)C6H3, 89°, -; 3,4-EtO(HO)C6H3, 218°, -; 3,4-(MeO)2C6H3, 226°, 100b; o-O2NC6H4, 192°, 96b; PhCH:CH, 294°, 58b; 3,4-(CH2O2)C6H3, 202°, -; 2,3,4-HO2C(MeO)2C6H2, 296°, 100b, 100c. II in dry Me2CO treated in a period of 2-3 hrs. with KMnO4 in dry Me2CO, the excess KMnO4 removed with NaHSO3, filtered, the Me2CO evaporated, and the residue crystallized from MeOH or EtOH gave 2-aryl-4-quinazolinones (III) (aryl, m.p., and % yield given); Ph (IIIa), 238°, 70; p-MeC6H4 (IIIb), 241°, 73; p-MeOC6H4, 208°, 50; p-MeOC6H4, 247°, 98; o-O2NC6H4, 237°, 95; m-O2NC6H4, 354°, 96; p-O2NC6H4, 365°, 90; 2,4-(MeO)2C6H3, 204°, 75; 2,4-(EtO)2C6H3, 174°, 87; 3,4-(MeO)2C6H3, 247°, 65;

3,4-(CH2O2)C6H3, 279°, 75; 3,4-EtO(MeO)C6H3, 239°, 90; PhCH:CH, 252°, 44 (cf. Stephen and Wadge, C.A. 51, 6649e). BzH (10.6 g.) and 15.1 g. o-H2NC6H4CO2Me in petr. ether (b. 60-80°) kept 3 days at 0° (CO2 atmospheric) and the product (75%) crystallized from petr. ether (b. 40-60°) gave o-PhCH(OH)NHC6H4CO2Me (IV), m. 77°. Similar condensation with p-MeC6H4CHO gave the corresponding o-[4-MeC6H4CH(OH)NH]C6H4CO2Me (IVa), m. 79°. IV and IVa kept 2 weeks at 0° in EtOH saturated with NH3 gave 41% IIIa and 58% IIIb. BzH (4 g.) and 10 g. o-H2NC6H4CO2Me warmed in 50 cc. EtOH containing a trace of HCl, and the orange solution refluxed 40 min. and filtered hot gave 8.6 g. white solid, m. 265-75°, yielding on extraction with Me2CO 6.9 g. insol. 1,2,3,4-tetrahydro-3-(o-carbomethoxyphenyl)-4-oxo-2-phenylquinazoline and 1.7 g. Me2CO-soluble (o-MeO2CC6H4NH)2CHPh, m. 188-90°. Refluxing 10.3 g. o-H2NC6H4CO2H and 12.5 g. 2,4-HO(EtO)C6H3CHO in EtOH gave 19.8 g. 2-[o-2,4-HO(EtO)C6H3CH:N]C6H4CO2H, m. 206°. Similarly were prepared the corresponding 2,4-EtO(HO) and 2,3-HO(MeO) analogs, m. 211° and 119°, in 97 and 80% yields, resp.

IT 60980-98-5
(Derived from data in the 6th Collective Formula Index (1957-1961))

RN 60980-98-5 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-methyl-5,6-diphenyl- (9CI) (CA INDEX NAME)

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ACCESSION NUMBER: 1957:9378 CAPLUS

DOCUMENT NUMBER: 51:9378

ORIGINAL REFERENCE NO.: 51:1971b-e

TITLE: A new synthetic approach to pteridines

AUTHOR(S): Osdene, T. S.; Taylor, E. C.

CORPORATE SOURCE: Princeton Univ., Princeton, NJ

SOURCE: Journal of the American Chemical Society (1956), 78, 5451-2
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

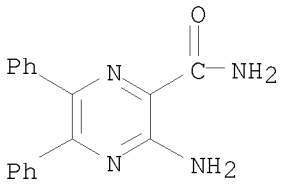
AB cf. C.A. 50, 13047b. A general method is described for the synthesis of pyrazine intermediates which permits the ready synthesis of 1-substituted pteridines. PhN2CH(CN)CO2Et with N2H4 or N2H4.H2O in EtOH yielded 3-hydroxy-4-phenylazo-5-aminopyrazole (I), m. 256° (decomposition). I with H in 98% HCO2H containing 10% Pd-C yielded 3-hydroxy-4,5-diformylaminopyrazole (II), m. 212-13° (decomposition). II with 50% H2SO4 yielded 3-hydroxy-4,5-diaminopyrazole sulfate (III). Cyclization of the N2H4 salt of nitrosocyanoacetohydrazide with 40% NaOH at room temperature yielded 3-hydroxy-4-nitroso-5-aminopyrazole (IV); catalytic reduction of IV yielded III. The same reactions with MeNHNH2 yielded 1-methyl-3-hydroxy-4,5-diaminopyrazole, m. above 250°. III with glyoxal, Ac2, and Bz2 yielded 3-hydroxy-1-pyrazolo [b] pyrazine (V), m. 314-15° (decomposition); 3-hydroxy-5,6-dimethyl-1-pyrazolo[b]pyrazine (VI), m. 325° (decomposition); 3-hydroxy-5,6-diphenyl-1-pyrazolo[b]pyrazine (VII), m. 269° (decomposition); 1-methyl-3-hydroxy-5,6-dimethyl-1-pyrazolo[b]pyrazine (VIII), m. 267-8°; 1-methyl-3-hydroxy-1-pyrazolo[b]pyrazine (IX), m. 242-3°. The

preceding compds. treated with Raney Ni yielded 2-amino-3-carboxamides. VII treated with Raney Ni 3 hrs. in boiling EtOH yielded 80% 2-amino-5,6-diphenylpyrazine-3-carboxamide, m. 203-5°. Similarly, IX yielded 2-methylaminopyrazine-3-carboxamide, m. 200-1°. Direct condensation of IV with Ac2 in EtOH containing Raney Ni yielded 2-amino-5,6-dimethylpyrazine-3-carboxamide.

IT 101445-25-4P, Pyrazinamide, 3-amino-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)

RN 101445-25-4 CAPLUS

CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



L7 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1956:69468 CAPLUS

DOCUMENT NUMBER: 50:69468

ORIGINAL REFERENCE NO.: 50:13047b-i,13048a-b

TITLE: Pteridines. XIV. Further studies on a new approach to pteridine synthesis

AUTHOR(S): Taylor, E. C., Jr.; Garland, Robert B.; Howell, Charles F.

CORPORATE SOURCE: Univ. of Illinois, Urbana

SOURCE: Journal of the American Chemical Society (1956), 78, 210-13
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 50:69468

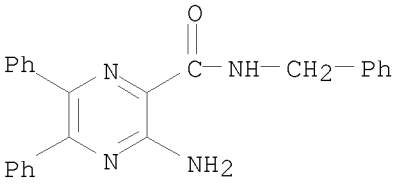
AB cf. C.A. 50, 2608h. 3-Amino-5,6-diphenylpyrazinamide (I) (1.509 g.) and 10 cc. BzCl refluxed 4 h., cooled, and diluted with 250 cc. petr. ether gave 1.179 g. 2,6,7-triphenyl-4(3H)-pteridinone (II), white needles, m. 290° (from CH2Cl2-petr. ether and then aqueous HCONMe2) (all m.ps. are corrected). The N-PhCH2 derivative (III) of I (0.5 g.) and 25 cc. AcCl refluxed 4 h. and diluted with 25 cc. petr. ether yielded 0.36 g. 3-acetylamino-5,6-diphenylpyrazinamide (IV), bright yellow platelets, m. 207-8° (from CHCl3-petr. ether). III (0.835 g.), 10 cc. Ac2O, and 10 cc. MeCN refluxed 4 h. and evaporated to dryness in vacuo, and the residue treated with EtOH and evaporated to dryness again gave 0.472 g. N-PhCH2 derivative (V) of IV, tan crystals, m. 149-50° (from CH2Cl2-petr. ether). V (0.613 g.) refluxed 3 h. with 0.5 g. Na in 10 cc. absolute EtOH and poured into 50 cc. H2O gave 0.503 g. III, m. 186-7°. 3-PhCH2 derivative of II gave similarly 93% III. I (2.53 g.), 5 cc. PhNCO, and 25 cc. dry pyridine refluxed 1 h. and cooled yielded 2.81 g. 3-(3-phenylureido)-5,6-diphenylpyrazinamide (VI), light yellow platelets, m. 240.5-1.5° (from aqueous EtOH and then aqueous HCONMe2). III (0.80 g.), 1 cc. PhNCO, and 10 cc. dry pyridine refluxed 2 h., cooled, treated with C, and diluted with petr. ether gave 1.03 g. N-PhCH2 derivative (VII) of VI, sparkling white platelets, m. 210° (from aqueous EtOH). VI (0.523 g.) and 7 g. polyphosphoric acid (VIII) heated 2 h. at 150° (CO2 was evolved), and diluted with 50 cc. H2O, and the precipitate sublimed at 200° and 2 mm.

gave 0.134 g. I, m. 204-5°; the sublimation residue sublimed at 300° and 2 mm. gave 3,5,7-triphenyl-2,4(1H,3H)-pteridinedione (IX), colorless solid, m. 327-8° (decomposition). III and VIII heated 45 min. at 150° gave 52% I and 63% VII. I (0.97 g.), 2 cc. PhNCO, and 10 cc. pyridine refluxed 3 days, cooled, diluted with 40 cc. $CH_2Cl_2$ and 250 cc. petr. ether, and filtered, and the filtrate evaporated to dryness gave 0.418 g. IX, white needles, m. 327-8° (decomposition) (from aqueous HCONMe2). III gave similarly 51% IX. I (1.52 g.), 3 cc. PhNCS, and 15 cc. pyridine refluxed 1 h., cooled, and diluted with 150 cc. petr. ether yielded 1.92 g. 3-(3-phenylthioureido) analog (X) of I, light yellow platelets, m. 233° (from aqueous HCONMe2). I (1.67 g.), 3 cc. PhNCS, and 15 cc. pyridine refluxed 3 days, cooled overnight, and filtered gave 1.87 g. 2-mercapto-3,6,7-triphenyl-4(3H)-pteridinone (XI), fine yellow needles, m. 301-2° (sublimed at 250° and 1 mm.). X heated similarly with PhNCS gave also XI. N-Bu derivative of I (2.70 g.), 3.5 cc. PhNCS, and 10 cc. pyridine refluxed 4 days, cooled, and diluted with 20 cc. $CH_2Cl_2$ and 100 cc. petr. ether yielded 1.49 g. 2-PhNH analog of XI, pale yellow crystals, m. 323-4° (from aqueous HCONMe2). I (1.34 g.), 2 cc. iso-PrNCS, and 20 cc. pyridine refluxed 2 days, cooled, and diluted with 20 cc. $CHCl_3$ and 100 cc. petr. ether gave 1.05 g. 3-(3-isopropylthioureido) analog (XII) of VI, white platelets, m. 251-2° (from $CH_2Cl_2$-cyclohexane). III (1.04 g.), 1.2 cc. iso-PrNCS, and 15 cc. pyridine refluxed 2 days and poured onto 200 g. ice yielded 0.7 g. N-$PhCH_2$ derivative (XIII) of XII, pale yellow crystals, m. 170° (from 70% AcOH). XII (1.24 g.) refluxed 6 h. with 1 g. Na in 25 cc. absolute EtOH, poured into 100 cc. $H_2O$, and filtered, and the orange solid digested with dilute HCl gave 0.174 g. 2-mercapto-3-isopropyl-6,7-diphenyl-4(3H)-pteridinone, light yellow needles, m. 270° (from aqueous EtOH); the filtrate acidified with concentrated HCl gave 0.72 g. 2-isopropylamino-6,7-diphenyl-4(3H)-pteridinone (XIV), bright lemon-yellow platelets, m. 324-5° (from aqueous EtOH). XIII (0.390 g.) refluxed 3 h. with 0.1 g. Na in 5 cc. absolute EtOH and poured into 50 cc. $H_2O$ yielded 0.30 g. 3-$PhCH_2$ derivative of XIV, sparkling yellow crystals, m. 305-7° (decomposition) (from aqueous HCONMe2). 3-Amino-5,6-diphenylthiopyrazinamide (XV) (1.1 g.) and 10 cc. BzCl refluxed 1.5 h., cooled, diluted with 50 cc. EtOH, refluxed 1 h., and evaporated to dryness, and the residue suspended in hot EtOH and filtered gave 2,6,7-triphenyl-4(3H)-pteridinethione, yellow crystals, m. 323-4° (sublimed). XV (1.23 g.), 3.4 cc. PhNCS, and 10 cc. pyridine refluxed 2 h., cooled, and diluted with 180 cc. petr. ether yielded 2.06 g. compound $C_{47}H_{33}N_9O$ (structure tentatively assigned), fine yellow needles, m. 369-70° (from aqueous HCONMe2), also obtained by refluxing the mixture for 3 days. It was recovered in 93% yield after refluxing 43 h. with concentrated HCl. XV (1.04 g.), 2 cc. PhNCS, and 10 cc. pyridine refluxed 36 h., diluted with 150 cc. hot petr. ether, and allowed to stand gave a small amount of unidentified, colorless needles, m. 72-157°, fine yellow needles, and cushions of orange prisms. The fine yellow needles and orange prisms recrystd. from pyridine-petr. ether yielded 1.15 g. 2-anilino-6,7-diphenyl-4(3H)pteridinethione, long yellow needles, m. 261-2°.

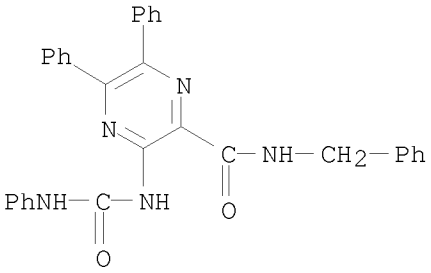
IT 7596-73-8P, Pyrazinamide, 3-amino-N-benzyl-5,6-diphenyl-
857180-32-6P, Urea, 1-[3-(benzylcarbamoyl)-5,6-diphenylpyrazinyl]-3-phenyl- 857180-53-1P, Pyrazinamide, 3-acetamido-N-benzyl-5,6-diphenyl- 857183-71-2P, Urea, 1-(3-carbamoyl-5,6-diphenylpyrazinyl)-3-phenyl-2-thio- 857993-08-9P, Urea, 1-[3-(benzylcarbamoyl)-5,6-diphenylpyrazinyl]-3-isopropyl-2-thio- 859297-19-1P, Pyrazinamide, 3-acetamido-5,6-diphenyl- 859300-58-6P, Pyrazinamide, 3-(3-isopropyl-2-thioureido)-5,6-diphenyl- 859300-59-7P, Urea, 1-(3-carbamoyl-5,6-diphenylpyrazinyl)-3-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 7596-73-8 CAPLUS

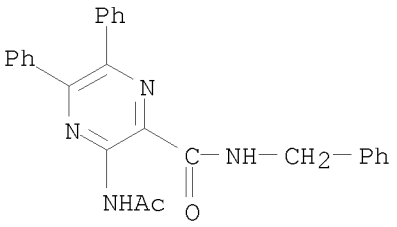
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



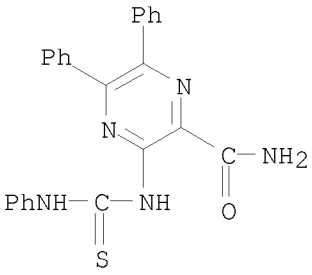
RN 857180-32-6 CAPLUS
CN Pyrazinamide, N-benzyl-5,6-diphenyl-3-(3-phenylureido)- (5CI) (CA INDEX NAME)



RN 857180-53-1 CAPLUS
CN Pyrazinamide, 3-acetamido-N-benzyl-5,6-diphenyl- (5CI) (CA INDEX NAME)

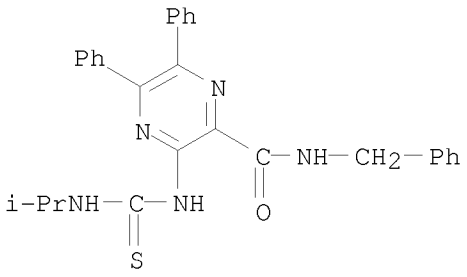


RN 857183-71-2 CAPLUS
CN Pyrazinamide, 5,6-diphenyl-3-(3-phenyl-2-thioureido)- (5CI) (CA INDEX NAME)

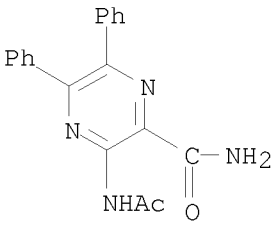


RN 857993-08-9 CAPLUS

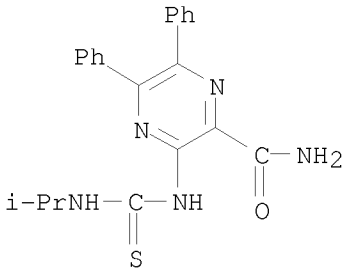
CN Pyrazinamide, N-benzyl-3-(3-isopropyl-2-thioureido)-5,6-diphenyl- (5CI) (CA INDEX NAME)



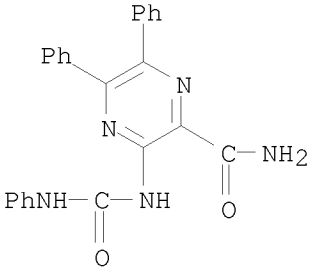
RN 859297-19-1 CAPLUS
CN Pyrazinamide, 3-acetamido-5,6-diphenyl- (5CI) (CA INDEX NAME)



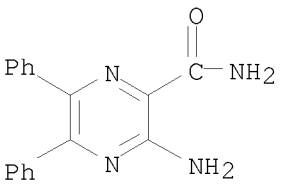
RN 859300-58-6 CAPLUS
CN Pyrazinamide, 3-(3-isopropyl-2-thioureido)-5,6-diphenyl- (5CI) (CA INDEX NAME)



RN 859300-59-7 CAPLUS
CN Pyrazinamide, 5,6-diphenyl-3-(3-phenylureido)- (5CI) (CA INDEX NAME)



L7 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1956:52652 CAPLUS
DOCUMENT NUMBER: 50:52652
ORIGINAL REFERENCE NO.: 50:10103e-g
TITLE: Route to 4-aminopteridines
AUTHOR(S): Taylor, E. C., Jr.; Paudler, W. W.
CORPORATE SOURCE: Princeton Univ., Princeton, NJ
SOURCE: Chemistry & Industry (London, United Kingdom) (1955) 1061-2
CODEN: CHINAG; ISSN: 0009-3068
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:52652
AB A new route for 4-amino-5,6-diphenylpteridines (I) is described. 2-Hydroxy-5,6-diphenylpyrazinamide (II) (Jones, C.A. 43, 3009h) gave 99% yield 2-chloro-3-cyano-5,6-diphenylpyrazine (III) when heated in a sealed tube with PCl3. III was also obtained in 80% yield by heating a mixture of II, POCl3, and PCl5. Fusion of III with guanidine carbonate, urea, or thiourea gave 65, 59, and 51% 2-amino, 2-hydroxy, and 2-mercapto derivs. of I, resp. III with N2H4.H2O gave 2-chloro-5,6-diphenylpyrazinoic acid hydrazide, or when repeated in the presence of KI gave 3-amino-5,6-diphenyl-1-pyrazolo[b]pyrazine. III gave 2-amino-5,6-diphenylpyrazinamide when treated with NH4OH and KI, or 2-amino-3-cyano-5,6-diphenylpyrazine when fused with NH4OAc.
IT 101445-25-4P, Pyrazinamide, 3-amino-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)
RN 101445-25-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



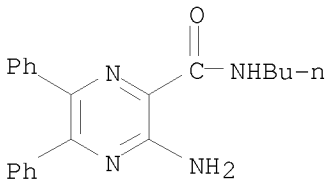

L7 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:25073 CAPLUS
DOCUMENT NUMBER: 48:25073
ORIGINAL REFERENCE NO.: 48:4553h-i,4554a-i,4555a-d
TITLE: Pteridines. X. A new approach to the synthesis of pteridines
AUTHOR(S): Taylor, E. C., Jr.; Carbon, John A.; Hoff, Dale R.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1953), 75, 1904-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 48:25073
GI For diagram(s), see printed CA Issue.
AB cf. C.A. 48, 2719c. A new synthesis of pteridines is described involving the preliminary synthesis of a 2,4(1H,3H)-pteridinedione (lumazine) by the conventional method and the subsequent aminolytic cleavage of the pyrimidine portion of the lumazine to give a 3-amino-N-substituted

pyrazinamide, followed by its ring closure to the desired pteridine. This method permits a much wider variation in the structure of the pyrimidine ring than does the conventional approach. Dry freshly distilled BuNH2 (100 cc.) and 15 g. 6,7-diphenyl-2,4(1H,3H)-pteridinedione (I) heated 12 h. in a sealed tube at 180°, the clear light brown solution treated with Norit, the excess BuNH2 removed in vacuo, and the residue diluted with 50 cc. hot EtOH and then hot H2O to incipient crystallization gave 8.8 g. (53.3%) 3-amino-N-butyl-5,6-diphenylpyrazinamide (II), bright yellow prisms, m. 146-7° (from CHCl3-aqueous EtOH). 3-Amino-N-benzyl-5,6-diphenylpyrazinamide (0.520 g.) in 20 cc. HC(OEt)3 (III) and 20 cc. Ac2O refluxed 5 h., and the solution evaporated to dryness in vacuo yielded 0.386 g. (72.3%) 3-benzyl-6,7-diphenyl-4(3H)-pteridinone (IV), white platelets, m. 248° (from CHCl3-petr. ether). II (1.0 g.) in 20 cc. 98-100% HCO2H and 20 cc. Ac2O refluxed 5 h., and the clear light yellow solution evaporated repeatedly to dryness in vacuo with 50-cc. portions of EtOH gave 0.337 g. (32.8%) 3-Bu analog (V) of IV, white platelets, m. 194-5° (from CHCl3-aqueous EtOH). II (0.50 g.), 20 cc. III, and 20 cc. Ac2O refluxed 5 h. similarly gave 0.396 g. (77%) V. 3-Amino-N-benzyl-5,6-diphenylpyrazinamide (1.0 g.) and 25 cc. ClCO2Et (VI) refluxed 20 h., and the resulting clear yellow solution evaporated repeatedly to dryness with 50-cc. portions of EtOH gave 0.996 g. (93.7%) N-benzyl-3-carbethoxyamino-5,6-diphenylpyrazinamide (VII), colorless prisms, m. 129-30° (from CHCl3-petr. ether). II (2.0 g.), and 40 cc. VI refluxed 20 h. gave similarly 1.539 g. (63.7%) N-Bu analog (VIII) of VII, colorless prisms, m. 110-11° (from CHCl3-petr. ether). VII (0.574 g.) and alc. NaOEt (from 0.5 g. Na in 70 cc. absolute EtOH) refluxed 20 h. gave 0.211 g. (40.9%) 3-benzyl-6,7-diphenyl-2,4(1H,3H)pteridinedione (IX), long colorless needles, m. 194-5° (from CHCl3-petr. ether). VIII (1 g.) similarly gave 0.80 g. (88.8%) 3-Bu analog of IX, long white needles, m. 246-7° (from CHCl3-petr. ether). 3-Amino-N-benzyl-5,6-diphenylpyrazinamide (X) (0.597 g.) and 25 cc. HCONH2 heated 3 h. at 190°, and the mixture cooled and diluted with H2O yielded 0.304 g. (64%) 6,7-diphenyl-4(3H)-pteridinone (XI), m. 297-8° (from aqueous HCONMe2), also obtained by refluxing X with HCONH2 containing 2 cc. dilute HCO2H. II similarly gave 52% XI. Me 3-amino-5,6-diphenylpyrazinoate (0.856 g.) in 75 cc. MeOH saturated with anhydrous NH3 at 0° and heated 1 h. at 120° in a sealed tube yielded 0.700 g. (86%) 3-amino-5,6-diphenylpyrazinamide (XII), m. 204-5° (from aqueous EtOH). XII (0.529 g.), 1.0 g. P2S5, and 15 cc. dry pyridine refluxed 1 h., the deep red solution cooled, poured into 200 cc. H2O, the resulting orange colloidal suspension dissolved by the addition of a small amount of 10% NaOH, the solution treated with C, filtered, and the filtrate acidified with glacial AcOH gave 0.304 g. (54.6%) 3-amino-5,6-diphenylthiopyrazinamide (XIII), orange needles, m. 158-60° (from aqueous EtOH). XI (2.975 g.), 4 g. P2S5, and 50 cc. anhydrous pyridine refluxed 2 h. similarly gave 2.34 g. (75%) 6,7-diphenyl-4(3H)-pteridinethione (XIV), bright red platelets, m. 270-80° (decomposition) (from aqueous HCONMe2). XIII (0.286 g.) in 10 cc. III and 10 cc. Ac2O refluxed 5 h. gave 0.164 g. (55.4%) XIV, bright red shiny platelets. XIV (0.5 g.), 1 cc. PhCH2NH2, 1 g. HgO, and 30 cc. EtOH refluxed 5 h., the mixture filtered, the black residue washed with 10 cc. hot EtOH, and the filtrate combined with the washings and diluted with H2O until crystallization began yielded 0.61 g. (99%) 4-benzylamino-6,7-diphenylpteridine (XV), light yellow platelets, m. 178-9° (from aqueous Me2CO). XIV (0.951 g.), 1.5 cc. BuNH2, 1 g. HgO, and 20 cc. absolute EtOH refluxed 2.5 h. similarly gave 0.870 g. (74.3%) N-Bu analog (XVI) of XV, bright yellow plates, m. 150-1° (from aqueous EtOH). XIV (2.0 g.) and 50 cc. absolute EtOH saturated with NH3 at 0° and heated in a sealed tube 10 h. at 130° gave 1.59 g. (84%) 4-amino-6,7-diphenylpteridine, light yellow needles, m. 175° (from aqueous Me2CO). Refluxing 0.924 g. XIV in 5 cc. CHCl3 and 20 cc. absolute EtOH with 0.8 g. HgO yielded 0.414 g. (33%) mercuric salt of XIV, light yellow crystals, m. 268-71° (from

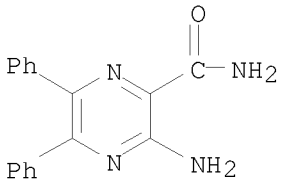
CHCl3-absolute EtOH). XV (0.20 g.) in 10 cc. 6N HCl refluxed 0.5 h. and the cooled mixture neutralized with NH4OH gave 0.14 g. (93%) XI, m. 297-8°. XI (88%) was also formed by hydrolysis of XVI. II (1.75 g.), 2.0 g. P2S5, and 25 cc. dry pyridine refluxed 1 h., the mixture cooled, poured into 150 cc. H2O, and the precipitate washed with H2O and recrystd. from absolute EtOH gave 1.54 g. (83.4%) 3-amino-N-butyl-5,6-diphenylthiopyrazinamide (XVII), bright yellow needles, m. 168-9°. XVII (0.635 g.), 0.7 g. freshly fused NaOAc, 10 cc. 98-100% HCO2H, and 10 cc. Ac2O refluxed 5 h. gave 0.441 g. (67.6%) 3-butyl-6,7-diphenyl-4(3H)-pteridinethione (XVIII), orange needles, m. 193-5° (from CHCl3-EtOH). XVII (1.53 g.) in 10 cc. HC(OEt)3 and 10 cc. Ac2O refluxed 3 h. yielded 0.962 g. (61.2%) XVIII. XVII (1.139 g.) in 30 cc. ClCO2Et refluxed 20 h., the solution evaporated to dryness in vacuo, and the residue evaporated 3 times with 50-cc. portions of absolute EtOH yielded 1.11 g. (77%) carbethoxy derivative (XIX), microcryst. orange solid, m. 173-4° (from CHCl3-EtOH). XIX heated 15 min. with 5 cc. 10% aqueous NaOH in 20 cc. EtOH gave 73% 1,2-dihydro-2-oxo derivative of XVIII, orange-red solid, m. 205-9° (from aqueous EtOH). XVIII (0.179 g.) in 1.5 cc. CHCl3 and 10 cc. absolute EtOH refluxed 6 h. with 0.2 g. HgO while a continuous stream of NH3 was passed through the mixture, the mixture filtered hot, and the filtrate evaporated to a small volume deposited 0.119 g. (69.8%) 3-butyl-4(3H)imino-6,7-diphenylpteridine, yellow platelets, m. 149-51°. 3-Amino-5,6-diphenylpyrazinoic acid piperidide (1.50 g.) in 50 cc. VI refluxed 5 h. and the mixture worked up in the usual manner gave 1.42 g. (79%) 3-carbethoxyamino-5,6-diphenylpyrazinoic acid piperidine (XX), yellow platelets, m. 174-5° (from aqueous Me2CO and then CH2Cl2-petr. ether). XX (0.50 g.) in 40 cc. EtOH saturated with dry NH3 and heated 6 h. in a sealed tube at 155°, the solution evaporated to dryness, the residue dissolved in dilute NH4OH, and the solution acidified with glacial AcOH gave 0.330 g. (90%) I, colorless microcryst. solid, m. 320-5°.

IT 7509-57-1P, Pyrazinamide, 3-amino-N-butyl-5,6-diphenyl-
101445-25-4P, Pyrazinamide, 3-amino-5,6-diphenyl-
110490-39-6P, Pyrazinamide, 3-amino-5,6-diphenylthio-
857180-46-2P, Pyrazinamide, 3-amino-N-butyl-5,6-diphenylthio-
857992-95-1P, Pyrazinecarbamic acid, 3-(benzylcarbamoyl)-5,6-diphenyl-, ethyl ester 857993-29-4P, Pyrazinecarbamic acid, 3-(butylcarbamoyl)-5,6-diphenyl-, ethyl ester
RL: PREP (Preparation)
(preparation of)

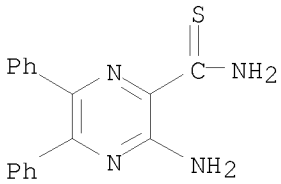
RN 7509-57-1 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-butyl-5,6-diphenyl- (9CI) (CA INDEX NAME)



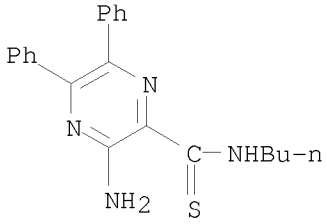

RN 101445-25-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



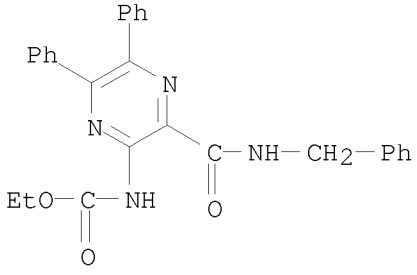
RN 110490-39-6 CAPLUS
CN Pyrazinamide, 3-amino-5,6-diphenylthio- (6CI) (CA INDEX NAME)



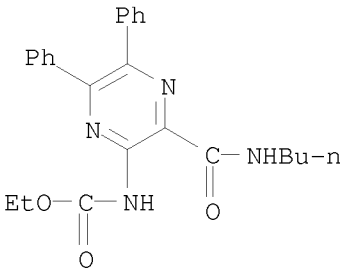
RN 857180-46-2 CAPLUS
CN Pyrazinamide, 3-amino-N-butyl-5,6-diphenylthio- (5CI) (CA INDEX NAME)



RN 857992-95-1 CAPLUS
CN Pyrazinecarbamic acid, 3-(benzylcarbamoyl)-5,6-diphenyl-, ethyl ester (5CI) (CA INDEX NAME)



RN 857993-29-4 CAPLUS
CN Pyrazinecarbamic acid, 3-(butylcarbamoyl)-5,6-diphenyl-, ethyl ester (5CI) (CA INDEX NAME)

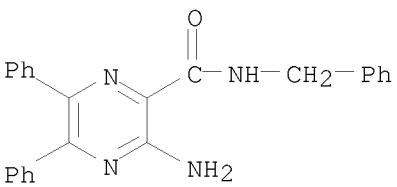


L7 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:14779 CAPLUS
DOCUMENT NUMBER: 48:14779
ORIGINAL REFERENCE NO.: 48:2719b-e
TITLE: Pteridines. IX. Hydrolytic ring cleavage of 3-benzyl-6,7-diphenyl-4(3H)-pteridinone
AUTHOR(S): Taylor, E. C., Jr.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1952), 74, 2380-1
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 48, 688c, 689g. 5,6-Diamino-4-hydroxy-2-mercaptopyrimidine (15.0 g.) in 300 cc. boiling water dissolved by the addition of 20% $Na_2CO_3$, the pH adjusted to 10 with dilute HCl, 80 g. wet Raney Ni added portionwise, the mixture refluxed 4 hrs., cooled, filtered, treated with 12.4 g. Bz2 in 100 cc. MeCOEt and 350 cc. EtOH, refluxed 8 hrs., acidified, and cooled yielded 13.2 g. 6,7-diphenyl-4(3H)-pteridinone (I), m. 297-8° (decomposition). I (0.5 g.), 30 cc. MeOH, 0.2 cc. $PhCH_2Cl$, and 0.16 g. KOH refluxed 2 hrs., and the mixture treated with 15 cc. 2 N NaOH and warmed yielded 0.483 g. 3-amino-N-benzyl-5,6-diphenyl-4-pyrazinamide (II), m. 188.5-89°. 3-Benzyl-6,7-diphenyl-4(3H)-pteridinone (III) in 30 cc. MeOH treated 0.1 g. KOH in 5 cc. water, and the mixture refluxed 10 min. and diluted with 5 cc. water yielded 64 mg. II, m. 188.5-89°. I (1.0 g.), 0.186 g. KOH, 3.8 cc. $PhCH_2Cl$, and 30 cc. MeOH refluxed 1 hr., and the mixture treated with 3 cc. AcOH and hot water to incipient crystallization yielded 0.26 g. III, m. 248°; dilution of the EtOH filtrate yielded 0.19 g. II, m. 187°; the mother liquor on dilution with 1 volume water yielded 0.195 g. I. In another experiment refluxing 24 hrs. yielded 0.21 g. III, m. 248°.

IT 7596-73-8P, Pyrazinamide, 3-amino-N-benzyl-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)

RN 7596-73-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

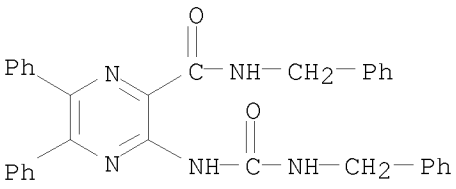


L7 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:3618 CAPLUS
DOCUMENT NUMBER: 48:3618
ORIGINAL REFERENCE NO.: 48:688c-i,689a
TITLE: Aminolysis of heterocyclic amides. I. The aminolysis of 6,7-diphenyllumazine
AUTHOR(S): Taylor, E. C., Jr.
CORPORATE SOURCE: Univ. of Illinois, Urbana
SOURCE: Journal of the American Chemical Society (1952), 74, 1651-5
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. following abstract An alkylamine with 6,7-diphenyllumazine (I) gives first an N-substituted amide of a 3-(3-alkylureido)-5,6-diphenylpyrazinoic acid, which can then be converted to an N-substituted amide of 3-amino-5,6-diphenylpyrazinoic acid by further reaction with the amine. The mechanism of these transformations is discussed and the results are interpreted as a substantiation for the ring cleavages previously postulated (cf. C.A. 47, 137h) in the reaction of 4-NH2 and 4-hydroxy-2-mercaptopteridines with alkylamines. I (3.0 g.) in 20 cc. PhCH2NH2 (II) refluxed 15 min. and diluted with 50 cc. absolute EtOH yielded 2.18 g. N-benzyl-3-(3-benzylureido)-5,6-diphenylpyrazinamide (III). EtOH, m. 88-93°; III m. 150-1°. III (0.60 g.), 10 cc. Ac2O, and 3 g. NaOAc refluxed 2 h., and the cooled mixture poured on ice and let stand overnight yielded III, m. 150-1°. III (0.50 g.) in 10 cc. II refluxed 8 h., diluted with 20 cc. EtOH, heated to boiling and diluted with water to incipient precipitation yielded 0.348 g. 3-amino-N-benzyl-5,6-diphenylpyrazinamide (IV), m. 188.5-9°; the filtrates from IV concentrated to 20 cc. and diluted with 20 cc. water yielded N,N'-dibenzylurea (V), 168°. I and II refluxed 8 h. yielded directly IV and V. H2SO4 (2 cc.) added slowly to 1.0 g. 3-amino-5,6-diphenylpyrazinoic acid in 15 cc. absolute EtOH, the solution let stand 24 h. at room temperature, and poured into 75 cc. water yielded 0.91 g. Me ester (VI), m. 204-6°. VI (165 mg.) and 2 cc. II refluxed 10 min., diluted with 15 cc. 50% EtOH and cooled yielded 190 mg. IV, m. 188.5-89°. IV (1.0 g.), 20 cc. 85% HCO2H, 20 cc. Ac2O, and 1.0 g. NaOAc refluxed 5 h. and the solution evaporated to dryness yielded 0.42 3-benzyl-6,7-pteridin-4(3H)-one, m. 248°. I (0.50 g.) and 15 cc. morpholine refluxed 14 h. yielded 0.53 g. 3-(morpholinocarbonylamino)-5,6-diphenylpyrazinoic acid morpholide (VII), m. 262-4°. VII (1.0 g.) sealed in 20 cc. morpholine heated 12 h. at 140° and 6 h. at 190° yielded 0.64 g. 3-amino-5,6-diphenylpyrazinoic acid morpholide (VIII), m. 190.5-1°. I and morpholine heated 12 h. at 190° yielded VIII directly. I (3.0 g.), 30 cc. piperidine, and 10 cc. HCONMe2 refluxed 16 h., filtered, and the hot filtrate treated with boiling water to incipient turbidity yielded 1.67 g. 3-(piperidinocarbonylamino)-5,6-diphenylpyrazinoic acid piperidide, m. 215-17°. I (5.0 g.) in 50 cc. piperidine heated 20 h. at 200° yielded 3.8 g. 3-amino-5,6-diphenylpyrazinoic acid piperidide, m. 156°. I (0.50 g.) in 15 cc. HOCH2CH2NH2 refluxed 12 h. yielded 0.453 g. 3-amino-N-(β-hydroxyethyl)-5,6-diphenylpyrazinamide, m. 186.5-87°. I (2.0 g.) and 40 cc. NH4OH heated 16 h. at 185° yielded 1.67 g. 3-amino-5,6-diphenylpyrazinamide (IX), m. 203.5-5°. IX (0.3 g.) and 1 cc. II refluxed 15 min., diluted with 10 cc. EtOH, and hot water added to incipient crystallization yielded 0.31 g. IV. IX (0.06 g.), 5 cc. piperidine, and 2 cc. HCONMe2 refluxed 16 h. yielded 0.053 g. IX, m. 203.5-5°. p-O2NC6H4NHCONH2 (2.0 g.) and 20 cc. piperidine refluxed 8 h. yielded 2.43 g. 1-(p-nitrophenyl)-3-(piperidino)urea, m. 165-6°. I (1.0 g.) and

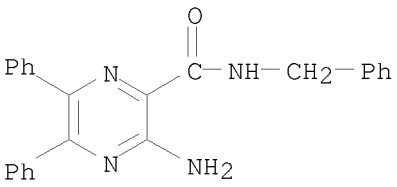
10 cc. 85% H4N2.H2O refluxed 6 h. and the mixture let stand 3 h. at 0° yielded 0.705 g. 3-amino-5,6-diphenylpyrazinoic acid hydrazide (X), m. 250-1°. The mother liquors from X evaporated to dryness, the residue washed with water, dried, extracted with CH2Cl2, and the extract diluted with petr. ether yielded 3-amino-6,7-diphenyl-2,4(1H,3H)-pteridinedione, m. 259-60° (decomposition); evaporation of the filtrates yielded about 0.015 g. X.

IT 7509-58-2P, Urea, 1-benzyl-3-[3-(benzylcarbamoyl)-5,6-diphenylpyrazinyl]- 7596-73-8P, Pyrazinamide, 3-amino-N-benzyl-5,6-diphenyl- 101445-25-4P, Pyrazinamide, 3-amino-5,6-diphenyl- 857180-39-3P, Ethyl alcohol, compound with N-benzyl-3-(3-benzylureido)-5,6-diphenylpyrazinamide 857183-65-4P , Pyrazinamide, 3-(2-hydroxyethylamino)-5,6-diphenyl- 857984-47-5P , Pyrazinoic acid, 3-amino-5,6-diphenyl-, hydrazide
RL: PREP (Preparation)
(preparation of)

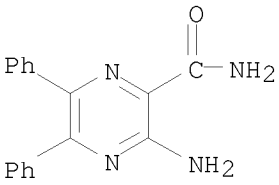
RN 7509-58-2 CAPLUS
CN Pyrazinecarboxamide, 5,6-diphenyl-N-(phenylmethyl)-3-[[[(phenylmethyl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 7596-73-8 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



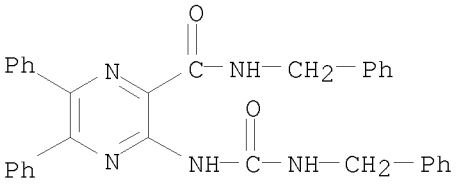
RN 101445-25-4 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5,6-diphenyl- (9CI) (CA INDEX NAME)



RN 857180-39-3 CAPLUS
CN Pyrazinamide, N-benzyl-3-(3-benzylureido)-5,6-diphenyl-, compd. with EtOH (5CI) (CA INDEX NAME)

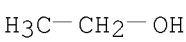
CM 1

CRN 7509-58-2
CMF C32 H27 N5 O2

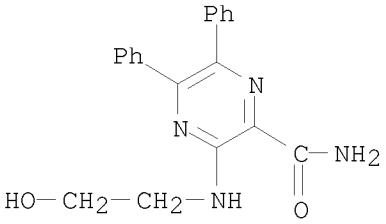


CM 2

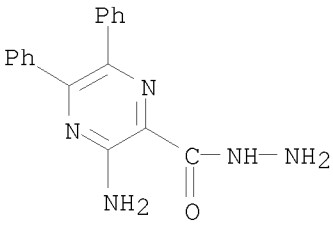
CRN 64-17-5
CMF C2 H6 O



RN 857183-65-4 CAPLUS
CN Pyrazinamide, 3-(2-hydroxyethylamino)-5,6-diphenyl- (5CI) (CA INDEX NAME)



RN 857984-47-5 CAPLUS
CN Pyrazinoic acid, 3-amino-5,6-diphenyl-, hydrazide (5CI) (CA INDEX NAME)



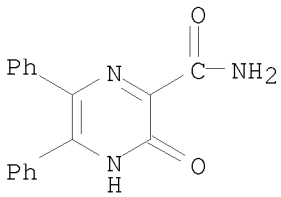
L7 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1949:15234 CAPLUS
DOCUMENT NUMBER: 43:15234
ORIGINAL REFERENCE NO.: 43:3009e-i,3010a
TITLE: Pyrazines and related compounds. I. A new synthesis of hydroxypyrazines
AUTHOR(S): Jones, Reuben G.
SOURCE: Journal of the American Chemical Society (1949), 71,

78-81
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB A general synthesis of 2-hydroxypyrazines (I) involves the condensation of 1,2-di-CO compds. with α-amino acid amides. H2NCH2CONH2 and (CHO)2 give 48% I, m. 187-9°. dl-Methionine Et ester (II) (287 g.) in 2 l. absolute EtOH, saturated at 0° with NH3 and kept 30 days, gives 175 g. (93% on basis of unrecovered II) dl-methioninamide (III), m. 48-9°. α-Amino-α-phenylacetamide (IV), m. 128-9°. H2NCH(CONH2)2 (V) (117 g.), added to 25 g. 40% aqueous (CHO)2 diluted with 25 mL. H2O, the mixture treated (temperature below 10°) with 10 mL. 12.5 N NaOH and, after several hrs., with 10 mL. AcOH, give 90% of the 3-carbamyl derivative of I, m. 265° (decomposition); a higher temperature or less (CHO)2 gives a smaller yield; KOH or Et2NH can be used in place of NaOH. AcCHO (36 g.) in 50 mL. H2O at -20°, treated with 60 g. V and then (dropwise, temperature below 0°) with 40 mL. 12.5 N NaOH, kept 18 h. at room temperature, and acidified with 50 mL. 12 N HCl, gives 59% 2-hydroxy-3-carbamyl-5-methylpyrazine (VI), m. 243-4° (decomposition); Ac2 gives 93% of the 5,6-di-Me analog (VII), m. 231-2° (decomposition). V (11.7 g.) and 21 g. Bz2 in 350 mL. 50% aqueous EtOH at 70°, treated with 10 mL. 12.5 N NaOH, give 83% of 2-hydroxy-3-carbamyl-5,6-diphenylpyrazine, m. 174-5°; 5-Ph analog m. 213-16°, 75%. 3-Me derivative of I m. 140-2°, 83.7%; 3,5-di-Me derivative m. 145-6°, 42% from MeCH(NH2)CONH2 and AcCHO; 3-methyl-5-Ph derivative m. 212-13°, 56.5%; 5,6-di-Ph derivative m. 225-7°, 97%; 5,6-di-Me derivative m. 199-200°, 11.3%. II and Ac2 in CHCl3 containing 1 equivalent piperidine give 70% (NaOH gives 88%) of the 3-(2-methylmercaptoethyl)-5,6-dimethyl derivative of I m. 128-9°; 3-(2-methylmercaptoethyl) derivative of I m. 96-7°, 97%. 3-Ph derivative of I m. 172-3°, 88.5%; 3-phenyl-5,6-dimethyl derivative of I m. 222-6°, 45%. p-HOC6H4CH2CH(NH2)CONH2 and (CHO)2 give 76% of the 3-(p-hydroxybenzyl) derivative of I, m. 212-13°; AcCHO gives 47% of the 3-(p-hydroxybenzyl)-5-Me derivative, m. 202-3°; Ac2 gives 77.5% of the 3-p-hydroxybenzyl-5,6-dimethyl derivative, m. 236-7°. VII (11.5 g.) in 75 mL. 3 N NaOH, heated several hrs. on the steam bath, gives 79% 2-hydroxy-5,6-dimethyl-3-pyrazinoic acid, m. 172-4° (decomposition); VI gives 30% of the 5-Me analog, m. 155-7° (decomposition); the 6-Me isomer, tan, m. 183-4° (decomposition).

IT 34121-79-4P, Pyrazinamide, 3-hydroxy-5,6-diphenyl-
RL: PREP (Preparation)
(preparation of)

RN 34121-79-4 CAPLUS

CN Pyrazinecarboxamide, 3,4-dihydro-3-oxo-5,6-diphenyl- (9CI) (CA INDEX NAME)

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For an explanation, enter "HELP LOGOFF".

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                    222.28     420.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -32.76     -35.88

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